THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 36 DECEMBER, 1936 No. 6

A BRIEF HISTORY OF THE DEPARTMENT OF ROENTGENOLOGY OF THE MASSACHUSETTS GENERAL HOSPITAL

By A. S. MERRILL, M.D.
MANCHESTER, NEW HAMPSHIRE

ON NOVEMBER 8, 1895, a German physicist, Wilhelm Conrad Röntgen, studying the effects of electrical discharges through vacuum tubes, perceived what had escaped the observation of previous experimenters. He discovered that from the tube emanated a light or radiation invisible to the human eye and hitherto unknown to man. It permeated substances opaque to all other known radiations, illuminated fluorescent materials, affected photographic plates like light and, most remarkable of all, cast upon a screen coated with fluorescent material shadows of objects of irregular density so that the dense portions were outlined within the lighter and could be made to impress these shadows permanently upon a photographic plate. He saw the dense bones of his hand on the screen and photographed them upon a plate. A new light had come into the world. He announced his discovery in December, 1895, and immediately throughout the world began the first flickerings of the light which has since grown to undreamed-of intensity.

The value of this new light to the medical world soon became apparent and everywhere experiments were pushed rapidly to increase its effectiveness in that field.

At that time the Massachusetts General Hospital in Boston was so fortunate as to count among its personnel an inspired and enthusiastic young man occupying the positions of head pharmacist and photographer. With his background of training in pharmacy and photography, his interest in electricity and a foresight nothing short of inspiration, he perceived the future value of the new radiation and immediately began investigating it. He assembled or built the necessary apparatus using discarded electrical equipment from other departments and bought an x-ray tube. Through no fault of his own the first experiments were not successful. The tube did not function. That probably accounts for the fact that this tube is still in existence and may be seen in the Department of Roentgenology of the Massachusetts General Hospital. He experimented with incandescent electric light bulbs with broken filaments because he had heard that roentgen rays could be produced from them. Again success eluded him. Nothing daunted nor dismayed, he purchased another x-ray tube. This time success rewarded his persistence and his first roentgenogram resulted. Thus the first experiments with the roentgen ray as a medical and surgical agent were made in the Massachusetts General Hospital by Walter Dodd within a month after its dis-

covery, and in the Department of Neurology of the old out-patient building his first successful application of the rays was made early in 1896.

The current for the tube was taken from a two plate static machine employed in electrotherapy and, as it was operated by hand, we can appreciate the untiring devotion of the unsung operator who turned the crank long enough to get results with the feeble tubes then in use. I imagine it was Joe Godsoe, Walter's assistant pharmacist and modest cooperator in all his early work, who turned the crank.

The surgical staff were enthusiastic over the results of the first experiments and roentgenograms of extremities immediately were in great demand.

Soon after this an "x-ray coil" was obtained as a loan through the generous interest of Professor Lemp of the General Electric Company and was installed in the old Kingsley studio at the corner of the brick corridor and the corridor to the lower wards. Cramped for space in both roentgenographic and dark rooms, unheated in winter and hot in summer, the work went on, spurred by the unflagging interest and devotion of Walter Dodd, and considerable routine service as well as experiments was accomplished.

Professor Lemp's machine was on exhibition at the fiftieth anniversary of "Ether Day" and excited so much interest that one of the trustees donated the money for its purchase. This machine was of the most recent design at that time with oil insulated coils and hammer-type interrupter. The Lemp coil was set up in the old West Room under the Bulfinch steps and the work profited by the change of location and apparatus.

During these experiments Dodd constructed a machine himself with an interrupter of his own design with which he made a satisfactory roentgenogram of an adult chest in ten seconds, but the main fuses could not stand the current consumed and the machine was condemned as unsafe.

At this time Dodd made what were probably the first recorded negatives of a case of osteitis deformans including most of the bones of the skeleton, and at a medical convention in Washington Dr. Reginald H. Fitz showed a roentgenogram of a whole skeleton. It was made in four sections, three with thirty minute exposures and one with thirty-five minutes, a total exposure of two hours and five minutes during which time the subject was obliged to remain completely immobile. Mr. Godsoe was again the uncomplaining victim and when the ordeal was over he had to be lifted and carried from the table.

The first item of expense for roentgen apparatus in the records of the hospital was for the purchase of a high frequency Kinraide coil bought in 1897. This seems to have been highly successful in some ways as it could be used as a portable unit and roentgenograms could be made with it at the bedside, but it was too powerful for most of the tubes then used and called for much experiment with different tubes. There seems to be no note at this time of appropriations for new tubes although we can believe that frequent replacements must have been necessary. In 1898 appears the note "X-ray appliances" $297.14, and in 1899 "X-ray appliances" $476.69. From 1900 to 1908 the average tube expense was $467.75 per year.

In 1903 Mr. Dodd and Dr. Seabury W. Allen made interesting studies on the influence of roentgen rays on the circulation. These studies were suggested by the report of an out-patient that the rays relieved the pain in osteomyelitis. They showed by blood counts that the number of leukocytes was increased in irradiated areas and observations of the circulation in an irradiated frog's foot led them to believe that the local blood supply was increased. They concluded that the relief of pain was due to changes in the character and amount of the blood supply. This discovery stimulated interest in treatment of disease.

For more than a year Dodd untiringly and assiduously worked at his ex-

periments, trying out more powerful apparatus, experimenting with new tubes and making roentgenoscopic observations and had, unaware of the unrecognized dangers of the radiations, exposed himself daily to unfiltered and unshielded roentgen rays, with the inevitable result that he developed severe reactions on both hands, and in November, 1898, was admitted to the hospital for the first of a long series of admissions and operations which eighteen years later culminated in his death.

In 1898 and 1899, the work increased gradually with growing success, and in 1900 the department was moved to better quarters where for the first time lead protection was used for the operator, and Dodd made experiments with water-cooled and oil-immersed tubes.

No further additions were made to the equipment until 1901 when Dodd designed and built a new machine which he presented to the hospital. With this he was able to explore hitherto uncharted regions of the human body and 2,538 roentgenograms and 900 roentgenoscopic observations were made for the surgical services in this year. No record was made of the use of the roentgen ray in medical cases.

In 1902 the increasing work, especially in radiotherapy, necessitated the purchase of three more machines, making six then in operation, and considerable superficial therapy was attempted, with gratifying results, but not until 1904 was a complete record system established. More than 20,000 cases had been admitted but they were recorded by name only. After this all cases were catalogued by name and diagnosis. During this year the first roentgenoscopic dark room was equipped replacing the old hand roentgenoscope and making possible more successful examinations and demonstrations of internal conditions, especially in the chest.

In 1907 two large roentgen machines were added to the equipment and considerable work was done on roentgenography of the nasal accessory sinuses.

For some time before this Dodd had recognized the need of medical training in his work and, in spite of his physical handicaps and otherwise busy existence, he had completed a regular course of study in the University of Vermont Medical School and received his M.D. degree. The Department of Roentgenology was officially established in 1908 and he was appointed Roentgenologist with the rank of Instructor in the Harvard Medical School. He resigned as pharmacist to the Hospital in the same year.

A friend of the Hospital donated several pieces of roentgen apparatus, among which was one which marked an important step in design. This was an interrupterless crossarm rectified unit designed by H. Clyde Snook of Philadelphia and the second of its kind in use. It was still in use when I left the Massachusetts General Hospital in 1924.

Fig. 1. Walter James Dodd. (From "American Martyrs to Science through the Roentgen Rays," by Percy Brown. Charles C Thomas, Springfield, Ill., 1936, p. 142.)

The records of the Department show a gratifying increase in the work during this period and in 1911, 6,000 cases were examined and an assistant roentgenologist became necessary. The Hospital is to be congratulated in having secured Dr. George W. Holmes in that capacity; this is further testimony to Dodd's wisdom in the management of the Department.

Dr. Holmes, with the cooperation of Dr. George Cheever Shattuck, did a great deal of work in the study of the heart and great vessels and developed a technique which became generally accepted in this country and which, with some modifications, is still in use.

In 1912 the Department again changed its quarters to the Gay Ward in the old surgical building and at last found itself in light airy rooms well adapted to its purpose. New equipment was acquired including an upright roentgenoscopic machine designed by Mr. Snook. This machine was well protected both for the operator and the observer. Dr. Dodd reported: "It is very gratifying to note that the medical service is making greater use of this department than ever before." He also emphasized in his report the importance of an accurate method of dosage measurement in therapy and made a plea for postoperative roentgen therapy in malignant disease and roentgen treatment of inoperable malignancy.

Mr. Sewall Cabot, who for some time had been experimenting on a machine that would give a non-fluctuating high potential type of current that could be measured satisfactorily for therapy, was invited to continue his work in the Department of Roentgenology with Dr. Dodd's cooperation and assistance. The machine promised to be successful and Mr. Cabot read a paper describing it before the American Roentgen Ray Society. Its value was somewhat nullified by Dr. Coolidge's invention of a new type of tube that produced the same results in a different and simpler manner.

After the installation of the new roentgenoscopic units, gastrointestinal study received a fresh impetus, and the economic and diagnostic advantages of roentgenoscopic study soon became apparent. The study by plates alone which was common in this country proved to be incomplete, cumbersome and expensive.

With the improvements in apparatus and technique, and the increasing reliability of the roentgen findings, work in roentgenology began to attract both undergraduate and postgraduate students in increasing numbers; in 1915, 684 students and physicians attended the clinics and the necessity of a definite teaching program was recognized. The expansion of the work, especially in the teaching and therapeutic branches, led to the appointment of a Resident House Physician for a service of one year with the same standing as residents in the medical and surgical services. He gave his full time in return for board, room and instruction. This was the first service of its kind in any American hospital and proved not only of great help to the Department but a valuable training for young physicians who intended to qualify for the specialty of roentgenology. It has always attracted a high class of conscientious young physicians who have been a credit to the Hospital and a factor in maintaining the ethical standards of roentgenology. The teaching of Dr. Dodd and Dr. Holmes could not but be an inspiring influence upon these pupils.

The outbreak of hostilities in Europe from the first attracted the attention of sympathetic members of the medical profession and many offered their services to the Allies. Among them was Dr. Dodd, who left with the first Harvard Medical Unit in 1915 and found opportunity to do much useful roentgen-ray work, especially roentgenoscopy, for the English and French armies. It is said that he joined the unit upon its departure so shortly convalescent from one of his surgical confinements that he had to be assisted to the ship. He returned in October, 1915, apparently much improved physically, but soon there were

recurrences of his lesions of roentgen-ray origin. He failed rapidly and died on December 18, 1916.

I have always considered myself fortunate in having known him during the last year of his life. His lovable nature, cheerful disposition, patience in difficulties, his happy and uncomplaining manner during his period of suffering were an inspiring and elevating influence to all who knew him. The nearest to a complaint that I ever heard him make was on one of his last visits to the clinic, which were becoming brief and irregular, when he told me "I am feeling pretty good today but I like to sit down more than I used to." The following extract from the report of the trustees expresses better than I can the place which he held in the hearts of his associates.

On December 18, 1916, the hospital suffered a great loss in the death of its Roentgenologist, Dr. Walter J. Dodd. Starting with nothing but high character and ability, he worked his way to a position of leadership and great usefulness. The fineness of his life was but emphasized by the pathos of his death. He had been connected with the hospital since 1892, first as Assistant Apothecary, then as Apothecary, and later as Roentgenologist. A pioneer in the use of x-rays he began to experiment immediately after Roentgen's publication in 1895. Like others of the early workers he was severely burned by the x-rays and cancerous disease followed. During the eighteen years following his first burns he underwent many operations and great suffering. His cheerful bearing of pain and his devotion to science are an inspiration to all the hospital. In spite of the difficulties and hardships of his early life, of the pain and distress of his later years, he became an acknowledged authority on x-ray interpretation, and under his leadership the Roentgenological department of the hospital grew from one occupying a previously unused space behind the stairs to one which requires eight large rooms and which during the past year has given aid to 17,616 patients. He went with one of the units to France, and it was said by his associates that his admirable interpretation of his excellent x-ray work contributed to a large extent to the very successful work done by the unit. His life was full of self-renunciation and service to others, and he died a martyr to the cause of science.

Although in many ways the loss of Dr. Dodd was irreparable, the Hospital found in the Department a man of high personal and professional qualifications, who had the added advantage of Dr. Dodd's training and inspiration, to carry on his work. Dr. George W. Holmes was appointed Roentgenologist to succeed Dr. Dodd and I was promoted from Resident to take Dr. Holmes' place as Assistant Roentgenologist.

During 1916 the volume of the work increased 50 per cent, largely in therapy and in the study of obscure medical cases. As a result of this, four more rooms, with an increase of staff, and two new roentgen units were added. The Assistant Roentgenologist was put in charge of the therapy with a special nurse to assist him and an increased number of patients were cared for in this department. Increase in demand for instruction in roentgenology resulted in 940 physicians and students visiting the Department in 1916 to study or observe and fourteen physicians were given instruction in cooperation with the Harvard Post Graduate School of Medicine. Nine fourth year students chose roentgenology as an elective and section teaching was given to the fourth year class twice a month.

On May 17, 1917, the Phillips House, private ward, was opened with complete roentgen equipment except apparatus for therapy, which was added later, increasing the work of the Department to a considerable degree. The general department was enlarged by the addition of three rooms in the old Gay Ward building and the construction of a lead-lined room for therapy.

During my absence with Base Hospital No. 6 in France Dr. James F. Boyd ably filled my place as Assistant Roentgenologist.

At this time due to the need of men for military service the specially trained men who had done all the technical work were replaced by graduate nurses who soon acquired proficiency in these duties and

filled the places so acceptably that most of these positions are still held by nurse technicians.

Courses in special training were opened to physicians wishing to specialize in roentgenology who were classed as Volunteer Assistants and who gave their services for a minimum period of two months, some remaining for a year or more. They received instruction and assisted the regular staff, gradually receiving more responsibility until they were assigned work of their own under the supervision of Dr. Holmes and were given some special subject for study and a thesis. Graduate nurses were admitted for a course in technical training and after a period of observation and teaching rendered considerable assistance to the regular technicians.

Reasons for economy during the war period restricted the work to cases of absolute necessity and in 1917 the number of cases was slightly less than the year before but larger than the average for the preceding three years. Two courses of instruction were given to members of the M.O.R.C. attended by fifteen officers and similar courses for the N.O.R.C. were attended by forty officers. Twelve physicians received postgraduate instruction and undergraduate teaching was given the third and fourth year students in sections. Study of fractures was encouraged by a fund donated by Mr. C. P. Beebe to equip an operating room with roentgen apparatus and a bedside unit was purchased for ward work.

The year 1917 saw a significant increase in gastrointestinal and genitourinary examinations, in the study of the heart and great vessels and of the lungs. Therapeutic work, though handicapped by inability to select cases and by the lack of radium, was carried on with encouraging results. Thirty-one cases of epithelioma, 30 cases of hyperthyroidism and 19 cases of inoperable and recurrent cancer were treated, and 24 cases of various scalp diseases, besides a good number of miscellaneous conditions.

In 1918 the number of patients increased slightly but the work was restricted to absolutely necessary cases for the duration of the war. The regular graduate teaching was continued and fourteen physicians received one month or more of postgraduate instruction. Lectures and clinics were given throughout the year to Army Medical Officers assigned to the Harvard Medical School and 246 recruits from the selective draft received chest or gastrointestinal examinations. During the influenza epidemic 106 chest examinations were made, adding important diagnostic data to the pathological picture of the disease.

An additional unit was purchased for the therapeutic department with money raised from the sale of used roentgen plates. The introduction of the Coolidge tube was of great value in therapy and demand for this service increased considerably.

In 1919, though restricted for economical reasons to absolutely necessary examinations, the number of cases increased 991 cases over 1918. I returned from military service and Dr. Boyd resigned to accept a position as roentgenologist to the Shannon Hospital in Providence, Rhode Island. The weekly undergraduate clinics were attended by a larger number than before and were made successful and popular by the preparation of these courses by Dr. Charles L. Martin. Twenty-seven physicians took the Harvard postgraduate course.

A room was equipped for therapeutic work and the resulting increase in this branch of the service soon necessitated a reorganization of this clinic. Conspicuous in this line of work were the dermatological and thyroid groups. It was arranged so that skin diseases could be treated with the cooperation of a dermatological consultant and Dr. C. Guy Lane was appointed in that capacity, with great improvements in the methods of treatment and closer harmony between the two departments of the Hospital.

With the able cooperation of Dr. James H. Means as medical, and Dr. Charles A. Porter as surgical consultant the thyroid clinic was put on a rational basis making possible the first controlled study of roent-

gen radiation in the treatment of toxic goiter. This was the original group clinic on which subsequent tumor clinics were modeled.

The year 1919 showed a large increase in the number of examinations of the chest, and of the teeth and skull, owing to the demand for complete physical examinations. There were more demands for roentgen therapy than the department could handle.

In 1920 and 1921 the amount of work increased greatly and changed in character. More examinations of medical cases were made and more cases treated. Space and apparatus were doubled and the whole department was systematized. Advantageous cooperation with other hospital departments was established.

In 1922 the Hospital was donated a workable amount of radium and rules for its distribution and use were established. The clinics for the therapeutic use of roentgen rays and radium were combined under the responsibility of the chief roentgenologist and additional space for this work was arranged.

From January 1 to December 31, 1922, 15,206 cases were examined and 3,419 treatments were given, including radium treatments. Dr. Holmes reported: "The number of obscure conditions requiring complete radiographic study has continued to increase. The difficult cases require the services of trained medical men and have increased considerably more than the simple cases which can be handled largely by technicians. We have been fortunate in being able to meet this increase with a voluntary staff." He spoke of the desirability of apparatus yielding radiations of very short wave length for therapy and advised the acquisition of such apparatus for the department. During this year the floor space of the department was doubled and new apparatus was acquired. The room arrangement was not ideal but was as satisfactory as could be expected.

Early in 1923 a short wave therapeutic outfit with an instrument for accurately measuring its output was acquired and put into operation in June of that year. At this time the department occupied sixteen large rooms with a staff of five full-time physicians and as many more consultants in therapy. Six nurses and students did the technical work. Five stenographers and clerks handled the records and reports. The daily number of patients averaged seventy-five.

The new therapeutic apparatus gave such encouraging results that it was employed to full capacity and a second unit was built for the Phillips House. Owing to the increase of work a Second Assistant Roentgenologist became necessary and Dr. Richard Dresser was appointed.

In May, 1924, I resigned my position as assistant roentgenologist, to take up private practice and the position of roentgenologist to the Elliot Hospital in Manchester, New Hampshire, and Dr. John D. Camp was appointed in my place.

An oil-immersed shock-proof roentgenoscopic unit was placed in the operating pavilion, proving of great value in fracture work. To the group of consultants in therapy a new one was added for gynecological conditions with Dr. Lincoln Davis as consultant. To facilitate radium therapy the following committees were appointed:

Radium Committee

Dr. George W. Holmes
Dr. Channing Simmons
Dr. J. Dellinger Barney
Dr. Frederick S. Burns
Dr. George A. McIvor

Radium Clinic

Dr. George W. Holmes, Chief
Dr. Robert B. Greenough
Dr. D. Crosby Green
Dr. George G. Smith
Dr. George R. Minot
Dr. C. Guy Lane

In 1925 no marked changes in equipment or personnel occurred. More cases needing complete roentgenological examination were received and relatively fewer simple routine cases. The Graham test came into

use the preceding year and in 1925, 261 cases were examined, with gratifying results. The total amount of work increased more than 1,000 cases over the previous year and the requests for examinations were greater than the department could handle. In connection with radiation therapy a tumor clinic was established and the demands for this service increased very markedly.

In 1926 the number of cases again increased appreciably and the amount of work increased relatively more owing to the growing demand for more complete and extensive examinations, and the position of Junior Assistant was created. The consultation service and the tumor clinic were of great advantage in the study of malignant cases. An arrangement was made with the Orthopedic Department for their House Officers to spend four months in the roentgen clinic.

FIG. 2. Staff Room, Department of Roentgenology, Massachusetts General Hospital, Boston, 1927.

In 1927 Dr. Camp was appointed Assistant Visiting Roentgenologist. For the reason that many patients reported to the roentgen clinic without provisional diagnosis or definite indication of what was desired, considerable study of symptoms and repeated examinations were necessary. An attempt to avoid delay and unnecessary examinations was made by having films developed and read as fast as they were made, stopping as soon as a diagnosis could be made or no further examination indicated. This made necessary a number of small dark rooms instead of one large one and called for considerable technical skill on the part of the medical and nursing staffs. Two new valve-tube rectified units were added in 1927, and two new examining tables and two small dark rooms were equipped. New apparatus especially adapted to genitourinary work was installed in the operating rooms and a deep therapy unit added. A weekly seminar conducted by the roentgen staff at which clinical, surgical or autopsy findings and roentgen studies of cases were discussed was instituted and was very valuable and popular.

In 1928 Dr. Camp resigned to accept a position at the Mayo Clinic.

Another dark room was added and a complete roentgen-ray unit installed in the genitourinary outpatient department. Several of the new line-focus tubes were purchased and gave satisfactory results. The increasing importance of accuracy in measurement of dosage in radiation therapy made it necessary to create the position of Consulting Physicist, and Dr. Howard O. Stearns was appointed.

In 1929 Dr. Dresser, who succeeded Dr. Camp, resigned to take the position as Roentgenologist at the Memorial Hospital in Worcester but retained a connection here as Assistant Visiting Roentgenologist. Dr. Hampton was promoted to Assistant Roentgenologist. The whole department was rewired with alternating current, all old type inflammable films up to 1925 were destroyed and a sprinkler system installed.

The opening of the Baker Memorial Hospital in 1930 for patients of moderate means brought a decided increase of work to the department. The technical and clerical staffs were increased but as this clinic took the full time of one physician and part time of another it was necessary to add to the medical staff. The Phillips House roentgen department was completely remodeled and equipped with apparatus standard with that of the rest of the hospital. Roentgenology assumed a more fitting relation in the Harvard Medical School by being transferred from a subdivision of surgery to a classification as a definite specialty in the Department of Medicine with a resulting change in undergraduate teaching. Postgraduate teaching also changed. The number of students for six or more months increased with a decrease of shorter term pupils.

No radical changes were made in 1931, 1932 and 1933. The amount of work increased and the high degree of service was maintained.

In 1932 little change was seen in the routine work of the department. Interpretation of films by the staff took place from 9 to 12 A.M., gastrointestinal examinations, routine roentgenoscopy and roentgenography throughout the day. The grouping of cases in the treatment clinic under various specialties was very satisfactory. The weekly seminar held every Wednesday from 4 to 6 P.M. continued to be very popular.

In 1933 the routine work proceeded as usual with increasing efficiency but no special changes were made and no major changes or additions were made in equipment. The term of service for residents was changed from one to two years because of the increase in the comprehensiveness of the field of roentgenology.

In 1934 evidences of the development of the department are seen in Dr. Holmes' report in which he outlines his policy of arrangement of the department in units grouped about the general roentgenologic center in such a manner that patients could receive the same careful and thorough study by the physician to whom they are assigned as they would get from him in his private practice. A room was equipped especially for the examination of chest cases, with pneumothorax or lipiodol injections. Undergraduate and postgraduate teaching continued as outlined in 1933.

During 1935 the general policy was continued with satisfactory results. The "pneumothorax room" was improved by the addition of a special table equipped for the study of the brain and spinal cord by encephalography. The weekly undergraduate clinics were held as in 1934 and the postgraduate class increased somewhat, nine physicians having taken the course. Among other research work there were observations on the effect of general body irradiation; development of a chair for encephalography; a new method for demonstrating bleeding peptic ulcers; the technique of spinal canal examination with lipiodol; location of kidney stones and diagnosis of tumors of the small bowel. The use of a condenser type of apparatus of very high speed for bedside work was introduced successfully. The relief method of examining the gastrointestinal mucosa was

demonstrated in a course of five lectures by Dr. Richard Schatzki formerly director of a department of roentgenology in Leipzig. This course was well attended by visiting roentgenologists. Similar courses on recent advances in roentgenology were advised for postgraduate instruction.

In this brief outline I have endeavored to trace the story of roentgenology in the Massachusetts General Hospital from its birth in the mind of Walter Dodd within a month of the announcement of the discovery of the x-rays by Röntgen to the present day.

Its growth has been steady and progressive from the day when Dodd made his first successful roentgenogram in the little room behind the stairs with Dodd and his assistant pharmacist, Joseph Godsoe, as the whole personnel, to the present when it occupies over 7,000 square feet of floor space in the central department with other rooms equipped for roentgenographic examinations in the surgical building and Out-Patient Department and complete separate plants in the Phillips House and the Baker Memorial with a personnel of thirty-nine, including one chief roentgenologist, three assistant roentgenologists, two residents, one graduate assistant, two consulting roentgenologists, one electrical engineer, one physicist, thirteen technicians, five clerks, five stenographers, two student technicians, two orderlies and one maid.

In this unavoidably dry and statistical sketch it is impossible to express the perspective of one who for nearly ten years enjoyed the privilege of sharing the work and associating daily with the men who were responsible for its inception and growth.

I cannot adequately do justice to the characters of these two men, Dr. Walter James Dodd and Dr. George Winslow Holmes, the former with his vision and foresight bringing this Department into existence, nursing it through its infancy and adolescence and finally giving his life for it, and the latter taking up the work where his predecessor laid it down and by his energy and keenness of vision and gift of organization bringing it to its present state of efficiency.

A just and comprehensive story of this work would be a character study of these two men and would require an abler pen than mine. Many of the readers of the contributions of the former pupils of Dr. Holmes share with me the privilege of acquaintance with both Dr. Dodd and Dr. Holmes and need no weak words of mine to picture them.

On this Twenty-Fifth Anniversary of Dr. Holmes' association with Roentgenology and the Massachusetts General Hospital, it is my pleasure to join in a tribute to a modest and unassuming gentleman who has traveled the way from a village schoolboy to a position of international authority in his chosen work.

Vol. 36, No. 6

THE RELIABILITY OF THE ROENTGENOGRAPHIC SIGNS OF INTRACRANIAL TUMOR*

By MERRILL C. SOSMAN, M.D.
BOSTON, MASSACHUSETTS

THERE are two methods of studying and analyzing material such as we are considering. The statistical result will vary with the method. One way is to take an entire group of confirmed cases and then review the roentgenograms to determine how many of them gave recognizable evidence of the presence of tumor. The other way is to keep records on a series of current cases and then determine how accurate one has been in predicting the presence and location of an intracranial tumor. The second method was used in this study. Obviously the first method will give higher percentages on the side of positive findings, for if one knows that a certain tumor was found in a particular location one may not hesitate to say that the variation from normal as shown in the roentgenograms was due to that tumor. On the other hand, if the report about to be made may be the deciding factor in a doubtful case then one naturally is careful to weigh the evidence and to attempt to evaluate it properly. Similarly, it is very difficult to estimate the part played by clinical judgment, based on experience, in making interpretations from a given set of films. It is our custom, in attempting to avoid the unconscious bias which may arise from a knowledge of the history or the physical examination in a given case, first to study our films without knowing anything about the patient. In this way one makes purely factual observations and proceeds to any conclusions justified by the findings. Only after this impartial survey has been completed do we consider the clinical signs and symptoms (if available). The next step is to correlate the evidence offered by the roentgenograms with that obtained by other means, or to weigh them in the balance with the weights determined by past experience and judgment, especially if the two are contradictory. Obviously one's accuracy increases with experience, and one's relative value in assisting the often long and involved course leading to a correct diagnosis is in inverse ratio to the clinical experience and judgment of the physician referring the patient for study. This will be referred to later.

Using the second method, then, as outlined above, we kept careful records of the series of skull roentgenograms during the last calendar year of Dr. Cushing's service at this hospital, but included patients from all of the services as well as from the neurosurgical division. There were 939 patients referred to us for roentgenographic examination of the skull and 1,219 examinations were made on this group. Some of the patients were followed into succeeding years to complete the study, but we included only the patients who had their first roentgenograms during that year. As a matter of fact, we made more examinations for the medical service than for the neurosurgical division, but with far fewer positive findings, as the patients referred from Dr. Cushing's service were highly selected and clinically rich material. We shall probably never again have such a wealth of clinical material as interesting, as fascinating, and as baffling as during the post-war years in association with Dr. Cushing.

As I have said and written before, our positive roentgenographic findings are divided into three classes of results, of increasing value to the neurological surgeon. They are (1) the general or nonspecific signs of intracranial tumor, such as evidence of increased intracranial pressure (increased convolutional markings more than normal for a given age, separation of the sutures, atrophy of the sella or of the sphenoid wings); (2) localizing signs of

* Based upon the "Report of the Roentgenologist," Eighteenth Annual Report of the Peter Bent Brigham Hospital, Boston.

tumor, such as local thinning of the vault or base, increased vascularity in one area, or displacement of the pineal gland, and (3) characteristic signs not only localizing but identifying the type of tumor present, such as the typical expansion of the sella due to a pituitary adenoma or the characteristic bony spicules, increased vascularity and local changes in the bone overlying a meningioma. If the roentgenologist can not only locate the tumor but also identify the histological type of tumor present, then he has done his utmost in helping toward a correct diagnosis. Our records were kept with these three features in mind, —the presence, the location and the type of tumor, with a definite statement written down in advance of operation or autopsy, often, in fact, before much of the history, clinical facts and laboratory findings were available. Our accuracy was then determined by the subsequent verification of a tumor, and only those histologically verified were counted in the determination, with separate notations for those verified only by clinical methods or by ventriculography. As an example of accidentally correct localization may I mention the case reported during that year of "localized increase in vascularity and slight thickening of the bone suggesting an underlying meningioma." As the location corresponded to the area indicated clinically, operation was undertaken with the expectation of finding a meningioma, but instead a glioma was uncovered, and the vascular area in the bone was found to be a small benign angioma of no importance whatsoever. Our score on that case was zero.

The greatest difficulty was in attempting to estimate the clinical accuracy for comparison with our percentages, and it is a dangerous and possibly unfair thing to do. Each patient was seen by several physicians, sometimes by many, and opinions at times were quite variable, occasionally diametrically opposite. For this phase of the work, however, we enlisted the aid of the resident in neurosurgery who knew the patients much more thoroughly than we could hope to do, and who knew the development of each case as the various sources of information were tapped and their contributions finally coördinated. With his help we feel that our figures are reasonably accurate for the clinical accuracy in this group of cases.*

Beginning with the general surgical service we find that nearly all of their skull cases were referred because of injury. It is practically routine to make roentgenograms in any case of injury to the head which has been severe enough to bring the patient to the hospital. It is unnecessary to repeat the stories of patients thought to have had only trivial injury who have died a few hours later. Everyone now knows the necessity of protecting the patient as well as the hospital and the clinical staff by having roentgenographic examinations made under such circumstances. But many physicians do not realize that insistence on immediate roentgenograms may be harmful rather than valuable, particularly in severely injured cases. It is more important to treat the patient for shock than to discover the size, number and distribution of the fracture lines. Furthermore, it is often difficult to obtain satisfactory films on a patient who is in poor condition or in a semistupor from alcohol, as are many of the injured brought in from the streets. Under these conditions a poor film with no evident fracture may lead to a false sense of security, whereas a good series of films secured under more favorable conditions might reveal a serious injury. Films *should* be taken in all cases, but not until the patient's condition warrants the necessary handling and manipulation incident to such a procedure.

In this group of cases, 167 in all, there were incidental and unexpected findings of one pituitary adenoma and one benign angioma of the bony vault, neither one confirmed by operation or autopsy.

By comparison the Medical Service sent

* Our thanks are due to Dr. Bronson Ray, Assistant Resident in Neurosurgery and to Dr. Hugh F. Hare, Assistant Resident in Roentgenology, for their invaluable help in this study.

us about three times as many patients for roentgenographic examination of the skull, more, in fact, than from the Neurosurgical Service. The interesting point in the group from the Medical Service was that 26 various brain tumors were reported, of which 18 were subsequently verified on the Neurosurgical Service. This group of patients, 413 in all, should be quite comparable to a similar group in any large hospital, as these patients were mostly from in or near Boston and did not come to this hospital because of its reputation as a brain tumor center. As there were 1,900 admissions to the medical wards this particular year, one would expect to find one brain tumor case in slightly over 100 admissions.

Still more interesting is the ratio of clinical diagnosis to roentgenographic diagnosis as shown in the following table.

TABLE I

MEDICINE

New Cases	413	
Re-examinations	30	
Total Examinations	443	
Verified Tumors		18
Clinical diagnosis, location		11
Clinical diagnosis, type		3
Roentgen diagnosis, location		12
Roentgen diagnosis, type		3

OTHER FINDINGS

Unverified calcified tumors or tumors with destruction of vault	8
Synostosis cranii	5
Paget's disease	7
Angioma of vault	1
Aneurysm internal carotid (unverified)	1
Calcification of internal carotid	14

This table shows that the accuracy of diagnosis as to the presence and location of an intracranial tumor was greater by roentgenographic methods (excluding encephalography and ventriculography) than by clinical methods, as used by a group of medical men who were not particularly "brain tumor conscious." By contrast similar studies on the next group of cases coming from the Neurosurgical Service shows that the percentage of clinical diagnosis was higher than the accuracy of the roentgenologists' diagnoses, confirming the statement made earlier in this paper as to the relative value of the methods as related to training, experience and judgment.

There were 363 patients referred from the Neurosurgical Service as "brain tumor suspects," and in this group there were 157 patients who were found to have an intracranial tumor of one sort or another. This group was particularly difficult to assay as the process of accumulating evidence leading to a correct diagnosis was more detailed, more varied and more elaborate than in the other groups. In some cases we had the benefit of the clinical findings, but in most of them the roentgen examination was done the day of admission, with only an abstract of the history to guide us. Similarly the neurosurgeons had our findings to help them, usually after the first day, so that an estimate of the clinical accuracy is less reliable than in the other groups. May I emphasize here that there was no competition in the sense of antagonism, but only the striving to do one's best in each case,—to contribute as much as possible, and to help in any way conceivable toward a correct diagnosis. We received as much (if not more) help and information for our own benefit as we contributed, and by mutual cooperation increased the value of the teamwork which is so essential in any complicated field of diagnosis or therapy. Of particular value were the frequent consultations in which discrepancies and conflicting evidence were ironed out and where

TABLE II

NEUROLOGICAL SERVICE

1. New cases roentgenographed	363	
2. Re-examination	130	
3. Total	493	
4. Verified tumors		157
5. Preoperative diagnosis, location		135—86%
6. Preoperative diagnosis, type		61—38%
7. Roentgen diagnosis, location		73—47%
8. Roentgen diagnosis, type		41—26%
9. Diagnosis definitely aided by x-ray		36—23%
10. Diagnosis entirely by x-ray		9— 7%
11. Diagnosis misleading by x-ray		6— 4%

in many of the cases some apparent fact or finding or opinion had to be discarded. It might well be noted here, with no attempt to boast, that the roentgenologist was the most consistent attendant at the neurosurgical operations and autopsies.

The statistical results in this group are given in Table II, and their analysis and explanation follow the table.

The number of re-examinations is quite high, as it was customary to have a set of films made at the time of discharge in each postoperative case. This is often of great value as it records the position of calcified areas and of the silver clips used for hemostasis during operation. If the patient returns with symptoms suggesting recurrence of the tumor, its location and size may be determined by the shift in position of the silver clips. Similarly the effect of radiotherapy can sometimes be demonstrated by the change in position of calcified areas or of the clips.

In this group the "Preoperative diagnosis, location" is the preoperative diagnosis by majority opinion or by authoritative opinion and includes all of the evidence in a given case, including the roentgenographic findings. The value of the roentgenographic findings alone is given in lines 9, 10 and 11. It was impossible to determine the clinical accuracy without the benefit of the roentgenographic reports, and unwise to attempt to do so as our method is only one of the many methods of examining a brain tumor suspect. After all, our objective is not to determine the accuracy of clinical diagnosis, but to calculate our own accuracy and the value of our contributions to the sum total in a given series of cases.

Line 7 "Roentgen diagnosis, location," is more reliable. In each case sent to us as a brain tumor suspect we summarize the roentgenographic findings in an "Impression," with a definite statement in the great majority of cases as to whether the findings indicate the presence or absence of an intracranial tumor. A mere statement of the structural changes is usually of little or no value unless they are interpreted in terms of gross pathology. By being as definite as is possible in a given case the roentgenologist helps not only the neurosurgeon, but also himself, provided he is able to learn by disaster as well as by triumph. Too many of us remember only our triumphs and quickly forget our mistakes,—a form of convenient memory which is not limited to our specialty.

Our findings, therefore, are put in writing and signed by the person responsible usually before most of the clinical and laboratory tests have been done, or their results known. It is astonishing, therefore, that we are able to predict the location of the intracranial tumor in almost one-half of the cases, and to guess accurately as to its histological type in one-quarter of them. This is a very decided advance in diagnostic accuracy as compared with the results in previous years and in different groups. It should be emphasized that these results are obtained from the study of plain films, stereoscopic, of course, and in different positions and directions, but not including encephalograms or ventriculograms. The latter are much more accurate, as will be shown in a subsequent table.

The 47 per cent which were diagnosed (located) by roentgenographic methods is made up of 17 per cent in which our findings were merely confirmatory, 23 per cent in which the diagnosis was definitely aided by our findings and 7 per cent in which the roentgenographic studies gave the most important evidence as to the presence and location of a given tumor. Not to be slighted or overlooked is the fact that in 6 cases (4 per cent) our films gave false or misleading signs suggesting an intracranial neoplasm, and in 49 per cent of the verified tumors there were no indications of its presence in the roentgenograms.

If we divide this group of verified intracranial neoplasms into their major subdivisions (the total number being insufficient for detailed analysis), we find marked variations in accuracy of diagnosis according to the type or location of the tumor, as follows (Table III):

TABLE III

VERIFIED INTRACRANIAL TUMORS

Pituitary adenomas	22
Diagnosed by x-ray	20–91%
Meningiomas	24
Localized by x-ray	16–67%
Acoustic neurinomas	17
Confirmed by x-ray	9–53%
Cerebellar tumors	24
X-rays compatible, not diagnostic	11–45%
Gliomas—in hemispheres	49
Localized by x-ray	14–28%
Calcification visible in x-ray	9–18%
Pineal displacement aiding localization, all cases	13
Pineal displacement misleading	1
Metastatic tumors verified	6
Pituitary adenomas verified by x-ray only	9
Calcified or destructive tumors—x-ray only	8

Of the 22 pituitary adenomas, 3 were not suspected clinically before roentgen examination. Two were not properly diagnosed by roentgenographic examination, one of them containing calcification extending above the sella being interpreted as a craniopharyngioma, and the other one being entirely suprasellar, with a pituitary fossa quite normal in size and shape. These suprasellar adenomas are more apt to give the chiasmal syndrome (bitemporal hemianopsia) than the glandular syndrome, and may be confused clinically and by encephalography with the small meningiomas arising from the tuberculum sellae. Similarly, the usual type of pituitary adenoma may undergo spontaneous calcification and may be misinterpreted as a craniopharyngioma, or the cessation of glandular activity which may be associated with the calcification in the adenoma may be misinterpreted as a result of radiotherapy. The greatest source of error is not in missing a pituitary adenoma, but in misinterpreting a sella deformed from general pressure as an adenoma. (In another paper[1] we are considering the pituitary adenomas more in detail.)

The meningiomas are of particular interest to the roentgenologist as so many of them show the characteristic vascularity, endostoses and local thickening in the overlying bone, enabling us to make a localizing diagnosis in two-thirds and a histological diagnosis in one-third of this group. These changes are most common, or most evident, when the meningioma is on the convexity of the brain. At the base of the brain the reaction is apt to be limited to one of dense hyperostosis, with no demonstrable increase in vascularity. This is particularly true of some of the very slowly growing meningiomas arising from the dura over the sphenoid ridge. Some of the meningiomas may reach an enormous size in relation to the brain without showing the usual roentgenographic signs of increased intracranial pressure, probably due to their slow growth. In general, the more slowly growing and therefore, more benign types will be associated with the largest or densest endostoses, and conversely the rapidly growing, more malignant type may cause a destruction of bone simulating a metastatic carcinoma. Meningiomas arising from areas not in close proximity to bone (e.g. falx, tentorium) may give no recognizable changes on the roentgenogram. Occasionally such a tumor may contain areas of calcification simulating a glioma. In another paper[2] we analyzed a larger group of these tumors, showing that about half of them will give evidence not only locating their point of origin, but also identifying them histologically. In this present group there were three other errors, the roentgenograms suggesting meningiomas where none were found,—one of them already noted earlier in this article.

The acoustic neurinomas can usually be diagnosed by the chronological development of the signs and symptoms, first those pertaining to the nerve itself and later the usual neighborhood or cerebellar symptoms, and by the physical examination. Roentgenographic examination, therefore, is as a rule only confirmatory, except when it establishes another diagnosis such as a metastasis or a meningioma in the suspected location. When positive, the typical findings are those of unilateral enlargement of the internal auditory meatus, with a funnel-shaped widening of the medial end of the acoustic canal. Both meati may be

enlarged in any case with chronically increased subtentorial pressure, and this must be differentiated from bilateral acoustic neurinomas, which occasionally occur. The most valuable position for an estimation of the size and shape of the acoustic canals and their internal meati is a direct anteroposterior view showing the petrous ridges in the center of the orbits. This may well be supplemented by a cerebellar view (Towne's position). Care should be taken in each view to obtain accurate positioning so that the two petrous ridges are symmetrical. Ventriculograms may be entirely normal even with an acoustic neurinoma large enough to give cerebellar symptoms.

The cerebellar tumors are by and large the most difficult to demonstrate roentgenographically of all the intracranial tumors. This is in part due to their position, the area being largely obscured by the mastoid shadows, and their character, being largely gliomas, not prone to undergo calcification. As a rule, we are able to demonstrate them only when they are calcified. There are nonspecific signs of increased intracranial pressure which usually appear fairly early with cerebellar tumors. Sometimes there is a backward tilting of the sella, with atrophy of the dorsum and forward bending of the posterior clinoids, but this may occur without cerebellar tumors. With slowly growing fairly benign tumors causing increased subtentorial pressure, the basi-sphenoid and basi-occipital bones may be quite concave instead of straight. There were 24 tumors in this group with roentgenographic findings reported as "compatible with cerebellar tumor" in 11 cases, or 45 per cent.

In the fifth and largest group, the gliomas, an occasional tumor may be located by localized thinning of the bone directly over the tumor. This is apparently due to increased pulsation in a vascular tumor and occurs only when the tumor is in or on the surface of the brain. The same appearance may be due to any vascular tumor so that it is of localizing value only. A larger number may be tentatively identified by particles of calcium deposited in the tumor,—in this particular group 18 per cent were so located. There is apparently nothing characteristic about the arrangement, distribution or size of the calcified areas to suggest the type of glioma present, but calcium deposits do suggest one of the more benign forms such as oligodendroglioma or astrocytoma. Strangely enough the *cerebral* medulloblastomas nearly always contain considerable calcium deposits and are relatively benign, in striking contrast to the *cerebellar* form of this tumor. It is quite possible that this tumor is wrongly classified. Occasionally an angiomatous tumor and rarely a meningioma may contain calcified particles of the type more commonly found in gliomas. A third method of *lateralizing* a glioma is the displacement of the pineal shadow, as determined from accurate anteroposterior or posteroanterior views. By careful measurements it can sometimes be determined that the pineal gland is also displaced anteriorly, posteriorly or vertically, thus further localizing the neoplasm. Pineal displacement is frequently of value in the gliomas. In this entire group of 157 verified tumors, measurable displacement of the pineal gland was of value in locating the tumor in 13 cases, and was misleading in one case. The latter was a patient with a small tumor blocking the aqueduct of Sylvius, with a resultant internal hydrocephalus. This in turn displaced the pineal gland downward and backward but not laterally, leading to an erroneous deduction of a midline frontal tumor. The correct diagnosis was promptly made after ventriculography.

The remaining entries of Table III are self-explanatory. They would raise our total and our average considerably if they had been verified by biopsy or by autopsy, but to include them without verification would defeat the purposes of this work.

The final group of cases to be analyzed is one in which ventriculograms were made. This method of direct tap of the ventricle or ventricles, removal of cerebrospinal fluid

and replacement by air, followed by suitable roentgenograms in at least four positions, was used 116 times. The following table gives our statistical results in this group, with explanations following the table.

TABLE IV

VENTRICULOGRAMS

Total examinations		116
Verified tumors after ventriculograms	62	
Tumors located correctly		59–95%
Failure due to unsatisfactory filling	2	
Incorrect localization	1	
Normal	21	
Tumors located, not verified	8	

Following the procedure in 116 cases, 62 tumors were verified. These were correctly located in 59, and in two of the failures the mistake could be attributed to incomplete filling of the ventricles, an error in technique for which we were not responsible. This leaves one positive error which occurred during my absence and which may be attributed to insufficient experience. In other words, this method is a very exact one when performed properly, but is associated with a very definite risk. I shall not attempt to discuss the mortality from this diagnostic method as it is entirely outside my field, and I doubt if anyone could give the accurate percentages in such a group, as an operation is the usual and immediate sequel when an accessible tumor is demonstrated. The 8 "tumors located, not verified" were mostly of the inaccessible type, a few deemed not operable for other reasons.

A final group, not numerically appraisable, is the one in which roentgenographic examination was negative in the face of clinical signs. This is frequently of value, as for instance, in patients with the local signs of pituitary tumor but with a normal sella, or again, patients with the signs and symptoms of a space-occupying tumor in a hemisphere but with normal ventriculograms. We can simply say that negative roentgenographic findings are often of value, sometimes of positive value, as well as of value in ruling out tumors, and beg the question of percentage.

In summary, we may expect to be able to locate 50 per cent and identify 25 per cent of all intracranial tumors by roentgenography. If ventriculography is resorted to, we should be able to locate practically all of the intracranial tumors large enough to give symptoms. The exceptions will be some of the subtentorial tumors, some small tumors in or around the optic nerves or chiasm, and small pituitary adenomas, ventriculography in the latter group not being indicated.

Our apologies are offered to Dr. Cushing for trespassing on his territory and my gratitude is expressed for his help and encouragement in our daily work. It is largely due to his stimulus that we have learned how to locate and identify most of these interesting and variable intracranial neoplasms.[3]

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THE HEALING OF LINEAR FRACTURES OF THE SKULL

By ROBERT G. VANCE, M.D.
BOSTON, MASSACHUSETTS

THE healing of linear fractures of the skull has been reported by Stewart,[1] Illig,[2] Schwarz,[3] and others. In spite of these reports there appears to be great diversity of opinion among roentgenologists concerning the healing of these fractures. Not infrequently one hears the opinion expressed that fractures of the skull always remain visible in the roentgenogram.

Complete disappearance of fractures in the skulls of children has been known to take place in a few months. Stewart reports the healing of such a fracture in six months, while Illig has observed complete healing of a fracture in the frontal bone of a child, five years old, in so short a time as four and one-half months. Illig reports other instances in which fractures in the skulls of children have disappeared in six months.

Attention should be called to the fact that fractures in the skulls of growing children have been seen to increase in width. Such a case is probably rare but has been noted by Stewart. It should also be noted that fractures in the skulls of adults have been known to remain visible over long periods of time. Illig reports a fracture in the skull of a man fifty-two years of age which was visible after fifteen years, although there was some evidence of repair.

In order to obtain more information concerning the healing of linear fractures of the skull we attempted, in two hospitals, to secure a re-examination of every case of linear fracture in which the original roentgenograms were at hand.

By confining the series to those cases in which the original films were at hand the possibility of an error in diagnosis would be obviated. Comparison of the two sets of films would also afford a means of determining at what time an old fracture may be differentiated from a recent one. This latter observation is sometimes of medicolegal importance. Any deposition of calcium in the brain or its coverings would be readily detected.

In all, 52 cases have returned for examination. Thirty-six had suffered a linear fracture of the skull more than two years previously. Every case in this group showed complete healing of the fracture line and there was no sign of injury remaining. The bones of these skulls were normal in appearance and there was no visible calcium deposit in the brain or its coverings.

Table I shows that each decade from the first to the fifth was represented and that the various bones of the skull were involved fairly evenly in frequency. The oldest case was that of a man fifty-two years of age at the time of injury. Twelve and one-half years later the fracture which had involved the right parietal and occipital bones had completely disappeared and the skull appeared normal in every respect. The earliest healing time in this series was in the case of a boy four years of age who showed complete healing of a fracture in the occipital bone in four months and twenty days.

Table II shows 7 cases in which the fracture lines are still visible but show sufficient repair to enable them to be recognized as old fractures. As healing takes place the margins of the fracture lines become less sharply outlined rendering the fracture line less distinct. As the healing process progresses, small spicules of bone may be seen bridging the fracture. There is no change in the density of the surrounding bone and there is no evidence of callus formation. Union is probably fibrous at first and this fibrous tissue later becomes ossified. When ossification is complete the fracture is no longer visible. The wider the fracture line, the longer the time required for healing.

Table I

Case No.	Age at Injury Years	Bones Involved	Healed After
1	5	Occipital	2 yr. 3 mo.
2	52	Parieto-occipital	1 yr. 6 mo.
3	9	Parietal	3 yr. 7 mo.
4	5	Occipital and frontal	1 yr. 10 mo.
5	7	Occipital	8 yr.
6	26	Frontoparietal	2 yr. 1 mo.
7	19	Parieto-occipital	4 yr. 3 mo.
8	31	Frontal	5 yr. 6 mos.
9	6	Temporoparietal	1 yr. 4 mo.
10	30	Temporoparietal	6 yr.
11	26	Frontal	3 yr. 6 mo.
12	14	Temporo-occipital	5 yr.
13	7	Parieto-occipital	3 yr. 1 mo.
14	33	Temporoparietal	7 yr.
15	11	Occipital	4 yr. 9 mo.
16	11	Temporal	3 yr. 3 mo.
17	6	Parietal	9 mo.
18	5	Frontal	11 mo.
19	4	Occipital	1 yr. 1 mo.
20	14	Parietal and temporal	1 yr. 5 mo.
21	42	Frontal	2 yr. 9 mo.
22	19	Occipital	4 yr.
23	15	Temporal	1 yr. 7 mo.
24	5	Parieto-occipital	1 yr. 3 mo.
25	28	Frontoparietal	3 yr.
26	13	Occipital	1 yr. 6 mo.
27	5	Parieto-occipital	7 yr.
28	7	Temporoparietal	1 yr. 9 mo.
29	41	Parietal	8 yr.
30	35	Occipital	3 yr. 3 mo.
31	5	Frontal	2 yr.
32	20	Frontal	3 yr.
33	21	Temporoparietal	2 yr. 1 mo.
34	9	Occipitoparietal	3 yr. 3 mo.
35	31	Temporal	2 yr. 3 mo.
36	4	Occipital	4½ mo.

Table II

TIME AT WHICH REPAIR WAS SEEN

Case No.	Age at Injury years	Bone Involved	Repair Seen At
1	6	Parietofrontal	11 mo.
2	5	Parieto-occipital	8 mo.
3	9	Occipital	16 mo.
4	20	Occipital	9 mo.
5	12	Frontal	5 mo.
6	31	Parietal	9 mo.
7	28	Frontal	10 mo.

TABLE III

CASES IN WHICH NO REPAIR WAS SEEN

Case No.	Age at Injury Years	Bone Involved	No Repair Seen At
1	5	Frontoparietal	5 mo.
2	30	Occipital	12 mo.
3	8	Parietotemporal	3 mo. 4 mo.
4	9	Frontal	2 mo. 4 mo. 5 mo.
5	5	Parieto-occipital	3 mo.
6	6	Frontal parietal and occipital	1 mo. 2 mo. 3 mo.
7	6	Occipital	1 mo. 2 mo. 3 mo. 4 mo.

In the skulls of adults it appears that about eight months is the average time required for sufficient repair to give the fracture line the appearance of an old fracture. In children the average time is shorter.

It is our present impression that fractures in adult skulls disappear roentgenographically in about two years. In children the time is much more variable but the average time is probably one year except in very young children where complete healing may take place in four months.

Three cases have returned in which there had been slight depression associated with the fracture and operation had been performed at the sites of the fractures. The duration of these fractures was three, four and six years. None of these fractures had healed completely except in parts remote from the site of operation. The removal of bone delays the union of the contiguous fracture line.

SUMMARY

Linear fractures in the skulls of adults may be expected to heal in about two years.

In very young children healing of linear fractures may take place in four months. In older children one year is about the average time at which healing is complete.

Linear fractures in the skulls of adults may be recognized as old fractures after about eight months.

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CHOLESTEATOMA IN CHRONIC OTITIS MEDIA

By A. S. MacMILLAN, M.D.
BOSTON, MASSACHUSETTS

AT THE Massachusetts Eye and Ear Infirmary during the ten year period from January, 1925, to January, 1935, 584 radical mastoidectomies were performed on patients with chronic suppurative otitis media. Of this number 288, or practically 50 per cent, showed macroscopic evidence of cholesteatoma. In 45 per cent of these 288 cases, enough definite cavitation could be made out on the roentgenogram taken in the usual Law position to make a preoperative diagnosis of cholesteatoma. Four years ago we added the use of the fronto-occipital view, by which we have been able to diagnose 68 per cent of our cases correctly. The remaining 32 percent showed no enlargement of the attic or mastoid antrum and no cavitation in the mastoid process to warrant a diagnosis of cholesteatoma.

FIG. 1. Showing the fronto-occipital position. The usual frontal-sinus head rest is used with the cassette inclined approximately 25° from the horizontal and the tube inclined about 15° toward the patient's feet. The patient is lying on the back with the chin flexed on the chest. As will be seen from the other illustrations, great accuracy is not necessary in this position.

Mygind,[6] over a seven year period from 1923 to 1930, performed 556 radical operations on chronic suppurative otitis media and found cholesteatoma present in 312, or about 56 per cent. In 97 cases, or less than one-third, cholesteatoma was suspected before operation.

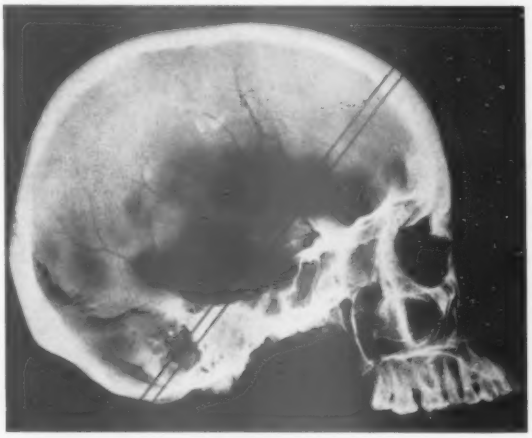

FIG. 2. Showing the projection of the antrum through the emissary vein region. Large emissary veins and extremely deep grooves in the bone, produced by the lateral sinus, should not be confused with the antrum. Law's position, which is always used in addition to this view, will aid in preventing this mistake.

The serious complications due to infection in the presence of cholesteatomatous cavitation in the temporal bone, such as labyrinthitis, brain abscess, perisinusitis abscess, meningitis, etc., are so frequent that once the diagnosis is made, otologists advise immediate operation. Very often the diagnosis can be made only by the roentgen examination.

The object of this paper is to call attention to the possibility of early diagnosis by the routine use of the fronto-occipital position in all patients giving a history of

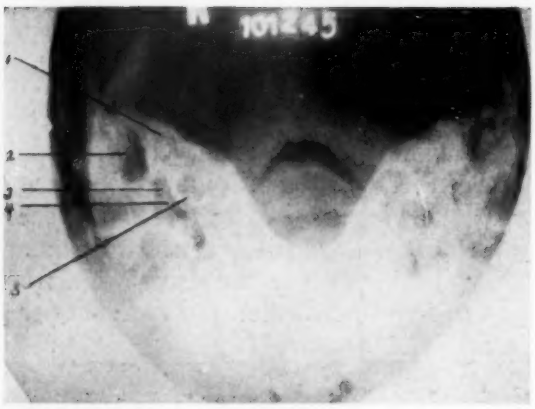

FIG. 3. This is the anteroposterior view of the temporal bone showing, *1*, the superior semicircular canal; *2*, normal sized antrum 6 mm. wide by 10 mm. high in a completely sclerosed mastoid, *3*, attic; *4*, middle ear; *5*, cochlea.

chronic otitis media. The position shown and described in Figures 1 and 2 is not new but has been more generally used in searching for fractures of the occipital region and later in studying the petrous pyramids in suspected infections secondary to acute otitis media.

Stereoscopic roentgenograms taken after the injection of the external canal with lipiodol aid greatly in the location of the structures seen in Figure 3, i.e., the ossicular chain, middle ear attic and antrum, semicircular canals, cochlea and the internal auditory meatus.

There are two types of cholesteatoma—the true and false, or primary and secondary. Grossly, and in microscopic appearance, they are identical, but they differ in their etiology.

The true or primary cholesteatomata are rare and were first described by Cruveilhier[2] in 1829. In 1838, Müller[5] described additional cases. Cushing[3] reported 15 in his 2,023 cases of brain tumor. Bucy[1] reported 3 cases arising within the diploe of the skull and collected 13 from the literature. They have occurred as spinal cord tumors and have been reported in the cecum and testicle. They are inclusion tumors of ectodermal origin, and when they occur, produce local symptoms and do not metastasize. Grossly they vary greatly in size and shape, are firm and pearly white. In cross section they show concentric layers of desquamated epithelial cells with cholesterin crystals between the layers. The actively growing and freshly desquamated cells are on the outside. There are no blood vessels.

The false, or secondary variety, with which we are concerned, may be found in the middle ear, attic, mastoid antrum, external auditory canal or the nasal sinuses. They have the same gross and microscopic appearance as the primary but differ in that they usually occur with chronic infection which may cause softening of the mass. Frequently they have a characteristic and very disagreeable odor.

Squamous epithelium is not normally found in the middle ear. There are two main theories as to its presence there. One is that there has been a transition from the cuboidal epithelium normally found here, to the squamous type as the result of chronic infection. The most commonly accepted theory is that there is an ingrowth of epithelium through a perforation in the membrana tympanum. The perforation usually associated with the formation of these tumors is through the posterior superior angle or Shrapnell's membrane. This is

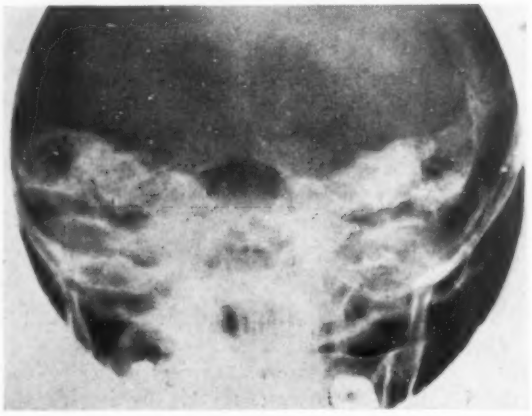

FIG. 4. Small undeveloped mastoids, whose cells are obscured in the Law position by the superimposition of the bony capsule, are seen to advantage in this projection; they in turn obscure the outline of the normal mastoid antrum.

the only place in the margin where a perforation can occur, because of the break in the continuity of the tendinous part of the drum. The epithelium of the posterior superior canal wall is said to be particularly rapidly growing. McKenzie,[4] in an excellent article, leans to the theory that these cholesteatomata are primary. As to the theory that the epithelium from the exterior canal grows in through the opening in the posterior superior angle, he says this theory "throws a severe strain upon one's credulity; and the strain is not reduced when we are virtually asked to believe that the only strip of epidermis, capable of producing cholesteatoma, is by an inscrutable dispensation of Providence led up to by the only perforation capable of using it."

Politzer in his book shows a microscopic picture of the mucous membrane of the external canal passing through the drum.

Regardless of which theory one accepts as to the formation of cholesteatoma Ziegelman[7] states that most otologists agree on the following facts: (1) that it is relatively common; (2) that it is dangerous; (3) that intracranial complications are prevalent; (4) that it has a great tendency to grow; (5) that it causes bone destruction and atrophy; (6) that a suppurative process is always around the cholesteatoma.

The roentgenographic examination of

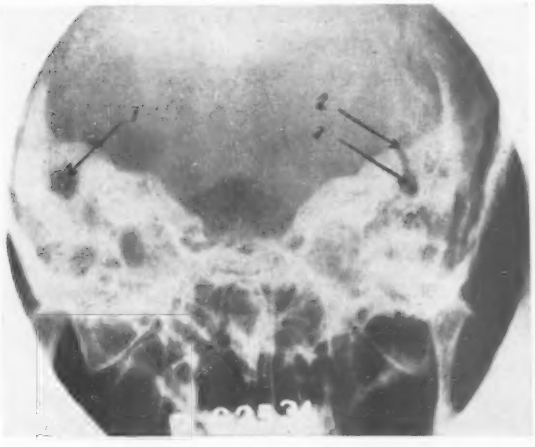

Fig. 5. *1*, shows a marked enlargement of the antrum; *2*, small emissary vein; *3*, normal sized antrum.

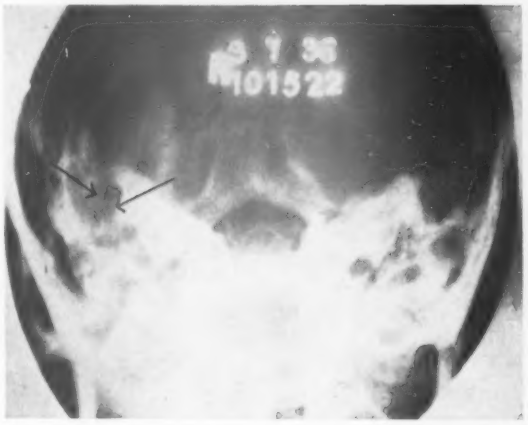

Fig. 6. Characteristic cholesteatoma cavity which was found empty at operation although the middle ear contained cholesteatoma detritus.

the sclerosed mastoid has always been rather unsatisfactory. Very little information can be given by the roentgenologist that the otologist does not already have. In the examination of the mastoid, in Law's position, the superimposition of the internal and external auditory meati is one of the principal requirements. This position shows the mastoid cells very clearly and the very important relation of the lateral sinus to the antrum; but in the sclerosed mastoid, because of the superimposition of part of the bony capsule over the mastoid antrum and the sclerosed cortex in the chronically infected middle ear, small and sometimes marked enlargements of the antrum cannot be appreciated. For this reason the anteroposterior projection is essential, for here there is no such superimposition. Because of the distance of the petrous pyramid from the surface of the skull, it was not until fine line focus tubes were available that sufficient detail of the structure of the petrous portion could be demonstrated satisfactorily.

The fronto-occipital position, in the normal pneumatic mastoid, does not show the mastoid antrum. The walls of the normal antrum are not clean cut because of the numerous openings in periantral cells (Fig. 4). The average size of the antrum in the completely sclerosed mastoid measures 6

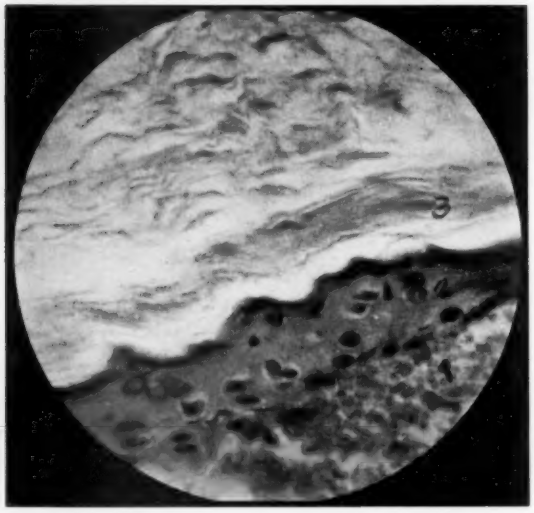

FIG. 7. Cross section of cholesteatoma showing, *1*, the hemorrhage beneath the living epithelium; *2*, the deeper columnar and surface squamous cells; *3*, successive layers of desquamated epithelium containing cholesterin crystals.

mm. in the transverse diameter and 10 mm. in the vertical (Fig. 5). Any increase in size of the antrum is due to erosion of the bone by the growing cholesteatoma. The density of the cholesteatoma itself as compared with that of the surrounding sclerosed bone is negligible. Films taken before and after the operative removal of the cholesteatomatous mass show no appreciable change in density in the region of the antrum. On two occasions, although cholesteatomatous material was present in the middle ear, operation showed the enlarged cholesteatoma cavity to be completely empty because the contents had been liquefied by infection and had drained out (Fig. 6).

These enlargements of the mastoid antrum cavity are usually very smooth in outline and that part of the cavity nearest the cortex of the temporal bone has a definitely eburnated wall. Large cholesteatomatous cavities may be multiloculated with projections extending down into the mastoid process; they may extend forward and upward into the squamous region; they may erode their way through the bone into the region about the lateral sinus or through the tegmen into the cranial cavity thus forming a definite bridge for infection to travel from the middle ear and produce serious complications. A fistula into the semicircular canal should be suspected when the cavity enlarges in that direction. Very large emissary veins and broad deep impressions in the bone caused by the lateral sinus must be considered and are not to be confused with the cavitation caused by a cholesteatoma.

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EVALUATION OF DENTAL ROENTGEN FINDINGS IN RELATION TO FOCAL INFECTION AND SYSTEMIC DISEASE

By HERMAN A. OSGOOD, A.M., M.D.
BOSTON, MASSACHUSETTS

THE part which focal infection plays in certain systemic diseases is well established and needs no further comment. Infection about the apices of the teeth is one of the most common sources of focal infection and because of accessibility, one of the most easily eradicated. Extraction of teeth on suspicion in the hope that the patient may be benefited is, however, unscientific and indefensible. Even the extraction of infected teeth is, as Pemberton[4] has pointed out, not always advisable.

Too radical extraction in an already weakened individual may produce an exacerbation of the original arthritic process which may entail great suffering.

Unfortunately, the tooth which shows definite local clinical evidence of disease is, as a rule, not the tooth which is important as a focus. It is the tooth with the "blind" abscess or pocket without local drainage which is the source from which bacteria and their toxins are absorbed into the blood and lymphatic channels, producing systemic complications elsewhere in the body. Such a tooth often presents no clinical symptoms or signs by which the dentist can identify it. Diagnosis must be based largely on roentgen findings. The interpretation of these findings depends first on careful technical detail, which is too often missing in busy clinics, and second on a knowledge of the anatomical structure of the tooth and its investing structures; and the change produced in them by disease.

These changes as seen in a roentgenogram are on an extremely small scale and too often cannot be visualized at all, unless a "slow" film and a fine focus tube, together with careful angulation of the incident ray, are used. The so-called "speed" films are too coarse and give too much contrast for accurate diagnosis.

The criterion of a diagnostic film is the demonstration of the black line representing the pericementum about the tooth, the lamina dura or socket wall, and the sharpness of detail of the cancellous structure of the alveolar bone.

Changes in roentgenographic density are relatively of less importance and too often

FIG. 1. Large bone cells about the root of the right lower first biscuspid.

are simulated by variations in the exposure or technique. Furthermore, there are wide variations in the density of the normal alveolar bone. A granuloma, for example, may appear as an area of increased roentgenographic density as compared with the more radiable antrum cavity, of diminished density when compared with average alveolar bone and even of the same density when compared with thin alveolar bone. In the latter case, diagnosis is based on changes in structure and line detail.

FOCAL INFECTION

Focal infection about the teeth may arise from one of four main sources: (1) infection of pulp in teeth which are still vital; (2) infected periodontal (pyorrhea) pockets;

(3) the walling off of infected material in pockets at the site of extracted teeth, and (4) infection at the tip (apex) of the tooth root.

The first group cannot be demonstrated roentgenographically, but teeth showing large cavities or leaky fillings should be suspected.

Periodontal pockets are foci which are commonly overlooked. They cannot be

Fig. 2. Granulomas at the apices of the right upper central and lateral.

kept clean except by constant dental attention. If the apical third of the root or the space between the roots in multi-rooted teeth is involved, extraction should be advised.

Walling off of infected material at the site of an extracted tooth is not an uncommon focus. The roentgenogram will show a cavity in the bone with or without partially absorbed bone fragments, and a bridging over by a bone shell at the alveolar margin. Such foci are simply removed by incision and curettage.

Infection at the tooth apex constitutes the group most likely to produce serious consequences. With a knowledge of the histological changes produced by the various lesions, it should be possible to translate them into their equivalents in terms of the roentgen picture. This in fact can be done in most instances, provided the film shows sufficient sharpness of detail.

Experience has shown that pathology at the tooth apex involves first the pericementum and lamina dura and then the cancellous bone. The first change which takes place is a widening of the black line of the pericementum at the apex, representing an actual thickening due to inflammatory congestion. The cause of this may be traumatic occlusion, congestion as the result of an inflamed or irritated pulp, or the first stage of abscess formation. Clinically, the tooth is raised and sore to bite on. If the cause is removed, the tooth may recover. Usually, however, the pulp dies and infection sets in. The second stage may be the development of an acute abscess or of a granuloma, depending upon the virulence of the infecting organisms and the patient's powers of resistance. The time interval varies from a few days in the former to several weeks or even months in the latter.

In the acute abscess, the first roentgenographic sign is cloudiness in the cancellous bone adjacent to the apex, and later thinning and finally loss of the lamina dura and of the trabeculae. The picture is similar on a small scale to the roentgen findings in a case of acute mastoiditis where we have first cloudiness, then thinning, and finally loss of the bone trabeculae. With complete destruction of the trabeculae, an abscess cavity is formed. Such cavities are not to be confused with large bone cells such as are seen particularly in the lower bicuspid and molar regions, with alveolar bone which may be normally thin and therefore shows increased radiability, or with shadows cast by normal anatomical landmarks or their distortions. If a sinus is established breaking through the buccal plate of the alveolus, a smaller darker circle may be seen within the area of bone destruction.

Prognosis for recovery by treatment without extraction depends on the establishment of drainage before there has been much destruction of the pericementum and denudation of the apex. Fairly large areas

of destruction in the cancellous bone but with little denudation of the apex have been observed to return practically to normal following treatment. Conversely, where the first roentgenogram shows considerable destruction of the pericementum over the apex prognosis is poor even though there is little involvement of the adjacent cancellous bone. As a rule, the untreated acute abscess goes on to a stage necessitating extraction. Occasionally, however, it subsides into a subacute or chronic form.

The granuloma type of reaction represents a connective tissue response to an irritation which may be bacterial or chemical. The granuloma, as its name implies, is a more or less sharply circumscribed connective tissue tumor. Since it represents not a destruction of alveolar bone but rather a replacement by connective tissue it may not show increased radiability. It can be recognized, however, by the loss of the pericementum and lamina dura at the apex and by the sharply defined margin of the lesion, which is circumscribed to the apex although occasionally it may extend down along the pericementum. Granulomas represent living connective tissue infiltrated with leukocytes and bacteria. They are highly vascular. Bacteria or their toxins, therefore, are readily absorbed into the circulation. It is extremely important that such lesions should be recognized. They are too frequently overlooked because they may fail to show the increased radiability which the roentgenologist is accustomed to associate with lesions at the apex of the tooth. The simple granuloma may undergo a normal repair if the root canal is cleaned out and adequately filled. It will then show nothing but a little residual thickening of the pericementum at the apex. Occasionally a granuloma, because of its size and interference with circulation, may undergo central softening forming within itself, if infected, an abscess cavity. The roentgenogram will then show erosion of the root tip which will not occur in the simple granuloma, and prognosis for treatment is less favorable. Occasionally a non-infected granuloma with central softening may form a cyst which is recognized by its sharp line of demarcation, its uniform fluid density, and when of appreciable size, its bone condensation line. Such a non-infected cyst does not represent a focus.

An acute abscess may occur at any age depending on the nature and virulence of the infecting organisms. Other things being equal, however, the acute abscess or granuloma, is more commonly seen in young in-

Fig. 3. Abscess with bone destruction arising from the apex of the right lower central and involving the apex of the left central.

dividuals whose resistance is high. In individuals who have passed middle life or in young individuals whose resistance has been lowered, the acute abscess may subside into a subacute or residual stage in which the eroded root tip becomes infected and forms a sequestrum which maintains chronicity. Such "blind" or chronic abscesses are of frequent occurrence in individuals of this type and may occur without having passed through the acute abscess stage. Nature attempts to wall off these chronic infections by scar bone (condensing osteitis) formation, which is rarely satisfactory or complete.

SCAR BONE

Such scar bone reaction, when occurring at the tooth apex, presents on a small scale a picure similar to that of osteomyelitis with sequestrum and involucrum formation as seen elsewhere in the body. In

this case the tip of the tooth root denuded of its pericementum and eroded by pus is in fact a sequestrum, and the scar bone reaction forms a definite involucrum at-

Fig. 4. Scar bone reaction associated with a chronic abscess.

tempting to wall off and localize the infectious process.

Scar bone, however, is not necessarily the result of infection; but rather results from a stimulation of the osteoblasts by an irritation which may be bacterial (chronic abscess), chemical (those used in root canal treatment), or injury (traumatic occlusion).

Scar bone reaction as a result of irritant chemicals is usually self-limited and localized at the apex of the tooth which has been treated. There may be some pericemental thickening, but there is no denudation or erosion of the root tip.

Scar bone as a result of traumatic occlusion is laid down on the alveolar side of the pericementum and represents Nature's attempt to reinforce the socket to meet the increased strain. This is in contradistinction to hypercementosis which results from stimulation of the cementoblasts and is laid down on the root side of the pericementum. Such scar bone reaction has, as a rule, no systemic significance. It is the result of wear and tear and is most commonly seen in patients showing similar hyperplastic changes about the margins of the vertebrae or other joints elsewhere in the body.[3]

There are, however, areas of sclerotic bone which apparently have no connection with dental pathology. Such areas occur commonly in the mandible, particularly in the bicuspid and molar region, and may lie between the tooth roots or several millimeters below them. They may vary in size from a pin point to a mass as large as a tooth. They have no clinical significance except in the rare instance where they may cause pressure irritation on a nerve.

The evaluation of the scar bone type of reaction, therefore, depends upon the identification of its cause. If it occurs as a result of infection it indicates chronicity, or, in other words, an attempt to wall off a process which cannot be healed by resolution, or a fragment of dead bone which cannot be exfoliated. As previously stated, this type of reaction has been found most commonly in patients whose resistance to infection is low and may be considered a criterion. The roentgenologist, therefore, should take a stronger position in advising extraction when this type of reaction is present,

Fig. 5. Scar bone of no clinical significance.

subject, of course, to the patient's ability to withstand the operation and its after effects. Such operations should be considered as "lightening the toxic load." Marked improvement in chronic cases should not be expected, because in many instances such lesions develop as a result of the patient's systemic condition, and are not its cause.

DEVITALIZED TEETH

Pemberton[4] states, "The day is past when, in the presence of refractory arthritis, an important tooth should be sacrificed merely because it is not vital."

Each tooth should be considered on its own merits. A pulpless tooth, furthermore, is not necessarily a "dead" tooth. Under favorable conditions the dental pulp can be aseptically removed and the root canal filled and sealed.

The pericemental attachments and investing structures may be undamaged and may remain vital. This will be evidenced in the roentgenogram as a pericemental black line of normal width and an intact lamina dura and cancellous bone at the apex. Such a tooth need not be extracted. Active periapical infection of clinical significance should produce histologic changes in these structures sufficient to be recognized in a clear sharp roentgenogram.[2]

Adequate pulp removal because of technical difficulties is limited, except in the hands of experts, to the anterior single rooted teeth. The roentgenologist should note whether the root canal filling (usually a gutta-percha point) extends to the apex, and whether it is in contact (sealed) to the side walls of the root canal. A canal filling which shows a space between the gutta-percha point and the canal walls is worthless. Such a tooth is always a potential menace since the seepage of moisture into the pulp canal forms an ideal culture chamber for bacteria. Where adequate root canal treatment has been carried out many teeth have remained in a satisfactory condition after pulp removal.[1]

CONCLUSIONS

One should remember first that the teeth, while the most accessible, are by no means the only source of focal infection; and second that the problem is primarily one of resistance and immunity. Many patients show infection about their teeth and yet have no evidence of systemic disease resulting therefrom. Furthermore, the local pathology about the teeth may be the result of a general systemic condition or lowered resistance, and not the cause.

The type of reaction as seen in the roentgenogram will indicate in general whether

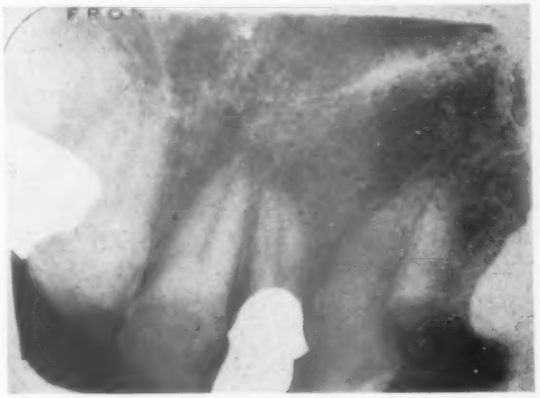

Fig. 6. Apical pericementitis on vital tooth due to occlusal strain.

the patient's resistance to infection is high or low. The granuloma type of reaction occurs more commonly in young adults whose resistance is high. There is usually a definite time relationship between the death of the pulp in the tooth under consideration and the onset of systemic symptoms. Removal of the dental focus will, if the systemic symptoms are recent, usually give relief. The blind or chronic abscess with scar bone reaction occurs more commonly in individuals of lowered resistance. Removal of such a focus will help to "lighten the load" but one should not expect too much improvement.

Prognosis after treatment depends first upon the type of region, second on the amount of denudation of the pericementum and erosion of the root tip. Acute abscesses and granulomas may undergo repair when their cause has been removed. Chronic abscesses with scar bone formation may be walled off but rarely repaired. Extensive denudation of the root tip is an unfavorable sign even though the amount of destruction in the adjacent alveolar bone is small.

A tooth from which the pulp has been removed should not be considered a "dead tooth" if its pericemental attachments and

investing structure are normal. Any pathologic process of clinical significance should show localized changes recognizable in the roentgenogram. If no such changes are present and the root canal is filled and sealed, extraction of the tooth should not be advised in the absence of definite clinical signs.

Finally, no diagnosis should be attempted from films which do not clearly show the pericementum and lamina dura. If the hospital or clinic is not equipped for accurate dental roentgenography, it is preferable to refer the patient to a dentist who has proper equipment and is trained in dental roentgen interpretation.

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CHRONIC PNEUMONIA IN YOUNG INFANTS*

By STEVENS S. SANDERSON, B.S., M.D.
DETROIT, MICHIGAN

PNEUMONIA in young infants may be divided into three general classes. First, there are the acute infections, then the pneumonia of primary tuberculosis, and last the chronic pneumonias. In the present discussion we are not concerned with the acute infections and will confine our attention to the roentgenological manifestations of the chronic forms.

The initial infection by the tubercle bacillus has been the subject of considerable study and a voluminous literature has accumulated. It is generally accepted that the bacilli, having found their way to the lung alveoli, set up an inflammatory process with the formation of a tubercle. After a period of incubation, which is said to be fairly constant at three to seven weeks,[10] the original focus becomes rapidly surrounded by an exudative infiltrate. This is an allergic reaction and varies in size within wide limits, sometimes occupying almost an entire lobe, commonly the upper lobe on the right, and at other times barely visible on the roentgenogram. At this time the tuberculin reaction is said to become positive.[10] The infection quickly spreads along the lymphatics and enlarged tracheobronchial nodes soon appear. The pulmonary manifestation is a true bronchopneumonia[1] and at this stage is not characteristic of tuberculosis when examined under the microscope.[10] This explains to some extent the difficulties encountered in interpreting roentgenograms of infants with pulmonary lesions. Chadwick[1] states that the presence of "definite uncalcified tracheobronchial nodes with clear cut margins sharply defined by the lung tissue associated with the parenchymal infiltration" is confirmatory evidence of tuberculosis. Enlarged tracheobronchial nodes occur also in other pulmonary lesions,[8] but are usually less prominent than in tuberculosis.

In 1925, Laughlen[4] described 4 cases of pneumonia in which oil aspirated into the lungs was apparently the etiologic factor. Since Laughlen's paper, others have appeared from time to time in the American and foreign literature describing what has been called "lipoid pneumonia," "oil aspiration pneumonia," and "pneumonoliposis."[5] Ikeda[3] and Pierson[6,7] have recently published excellent articles on this subject, reviewing the literature and presenting clinical, pathological, and experimental data. Ikeda presents evidence in support of the claim that this condition should be recognized as a disease entity. He found all of his cases by reviewing autopsy material and it is probable that many of the chronic pneumonias in infants under two years of age will be found to fall in this group.

The similarity of this type of pneumonia to tuberculosis is pointed out by Pierson and he emphasizes the importance of serial roentgenograms. Mineral and animal oils are the commonest offenders, while vegetable oils excite little reaction in the lungs. Cod-liver oil and similar products, liquid petrolatum alone and in combination with other medication as nasal drops are the most common. Less frequently found are milk fat, egg yolk, olive oil, and amniotic fluid.[11] Holt and Howland[2] mention 2 cases diagnosed during life, later confirmed at autopsy. Twenty-one others seen by them and those recorded in the literature were all diagnosed at autopsy.

During the four months, May 20 to September 19, 1932, six infants, one and one-half to three months of age, were admitted to the Massachusetts General Hospital because of rise of temperature, failure to gain weight, cough (except Case II), dyspnea (except Cases V and VI), and either anorexia or vomiting. All had been fed cod-liver oil with a teaspoon, and one in-

* From the Department of Roentgenology, Massachusetts General Hospital, Boston.

fant (Case IV) had received "nose drops" five times a day over a period of four days. Roentgenograms of the chest in most cases revealed extensive areas of consolidation, chiefly in the upper lobes and about the hilus (Figs. 2 and 3). Only one film (Case II, Fig. 1) did not show this consolidation, and it was taken within twenty-four hours of the onset.

REPORT OF CASES

CASE I (No. 207585). K. S. W., white male, born March 18, 1932. He was a normal, full term baby, weighing 8 pounds. During the first two weeks he lost 13 ounces and vomited frequently. At eight weeks he weighed 9 pounds 5 ounces. Three days later, four days before admission, the infant developed a cough and was irritable, with a temperature of 101° F. on admission, May 20, 1932, he weighed 8 pounds 12 ounces and had a temperature of 101.8° F., the white blood count was 24,000, red blood count 2,960,000. The physical examination disclosed malnutrition, dyspnea, and decreased motion of the chest on the right. The right lung contained many fine, crackling râles. The left lung was clear. The abdomen was slightly distended and the spleen just palpable. The next day, coarse and medium râles were heard in both lungs, more on the right; dullness was noted posteriorly over the upper portion of the chest on the right. A roentgenogram of the chest showed increase in hilar markings, an area of consolidation in the right upper lobe becoming less dense as the periphery of the chest was approached and some mottled dullness in the upper left lobe. The baby was placed in an oxygen tent. Two days later the temperature reached a peak of 107° F., dropping later in the day, and gradually returned to normal in thirteen days. The chest signs on the ninth day were the same except for dullness over the left apex, posteriorly. They showed little change until the seventeenth day when it was noted that the dullness on the left had increased. Roentgen examination at this time showed an increase in both the size and density of the consolidation in the upper lobe on the right and mottled dullness along the lower right and entire left heart border. He had lost 4 ounces since admission. On the twenty-first day the oxygen tent was discontinued. His temperature was 99° F., he had gained 1 ounce and the left lung was clear on physical examination. One week later, both lungs were clear and there was a negative reaction to 0.01 mg. of tuberculin. The child's temperature was ranging between 99° and 100° F., with one isolated recording of 102° F. On the thirty-first day 0.1 mg. of tuberculin was given intradermally with negative result. He vomited his early feedings, he still had a loose cough, and his temperature was 102° F. Another roentgenogram of the chest showed decrease in the density of the upper right lobe and the perihilar regions. A small, triangular shadow was present at the lower border of the right hilus in the region of the interlobar septum which suggested a small amount of encapsulated fluid or thickening of the interlobar pleura. No change was noted in the width of the mediastinum. The following day his temperature was still 102° F.; bulging of the right ear drum was noted and paracentesis yielded a drop of pus. Three days later he began to gain weight and his temperature was again 99° F. During the following five days considerable improvement was seen, the child gained 1¼ pounds; another tuberculin test, 0.01 mg., was negative. He was seen in the Out Patient Department one month later and had gained 3 pounds, was taking his feedings well, and was not vomiting. His lungs were clear on physical examination. Through an error no roentgenogram was taken.

CASE II (No. 209844). R. K. L., white male, born June 10, 1932. He was a normal, but small, full term baby, weighing 5 pounds 12 ounces. One week after birth he developed irregular respirations, gained poorly, was apathetic, and rarely cried. After being put on a formula he seemed to do better. The day before admission he refused all feedings, breathing became labored, and his temperature rose to 101.2°F. On admission, July 24, 1932, he weighed 7 pounds 8 ounces, his temperature was unchanged, and the white blood count was 11,000. He was acutely ill with rapid, shallow, irregular respirations and flaring of the alae nasi. Chest was flattened on the right with narrowed intercostal spaces. The lungs were resonant and no râles were heard. A tuberculin test, 0.01 mg., was negative. A roentgenogram of the chest (Fig. 1) revealed a moderate increase in the density of the hilar shadows and a fine mottling throughout both lungs, least marked in the lower portion of the right lung. Another film taken the following day was essentially the same. On the fifth day showers of coarse râles were heard in both lungs and there was dullness

over the left base posteriorly. The temperature ranged between 99° and 100° F., being higher in the afternoon, and returned to normal on the seventeenth day. A roentgenogram taken on the eleventh day showed consolidation of the upper right lobe, except the apex, and the right and left perihilar regions. The periphery of the left lung and a portion of the lower right lung had cleared. The appearance was almost identical to the film of Case I taken on the sixteenth day. The following day there were exaggerated breath sounds noted anteriorly on the left, diminished on the right and showers of coarse râles over the right apex and left midlung, posteriorly. His weight was unchanged. Three weeks after onset the baby seemed well clinically except for failure to gain weight, and anorexia. Roentgen examination of the chest (Fig. 2) showed no change in the shadow on the right but a definite decrease in that on the left, chiefly the outer margin. After discharge on the twenty-fourth day, the infant was not seen again.

Case III (No. 210162). W. H. J., white male, born June 9, 1932. He was a small, normal, full term baby, weighing 5 pounds 9 ounces. Four days before admission he developed a cough, vomited, and refused most of his feedings. He lost weight. The next day pallor and rapid respirations were noted. The cough became

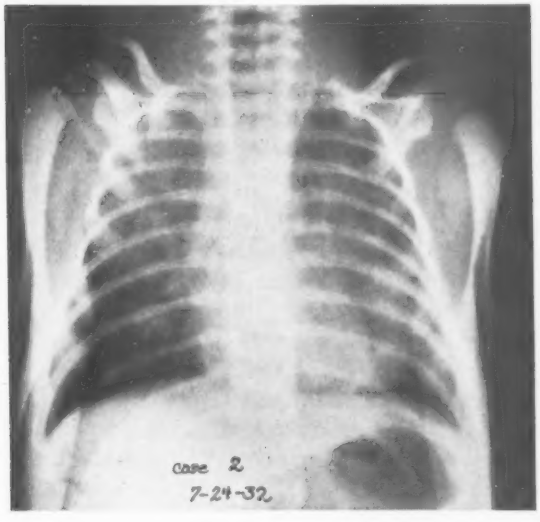

Fig. 1. Case II. Within twenty-four hours of onset. There is an extensive fine mottling throughout both lung fields, characteristic of bronchopneumonia. This mottling is least marked in the lower right lobe.

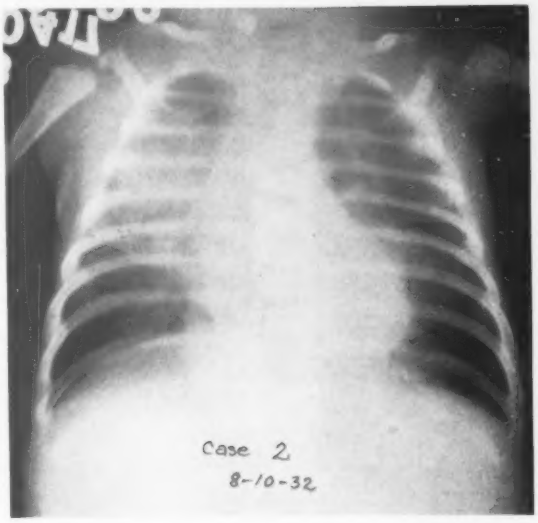

Fig. 2. Case II. Eleventh day of illness. Consolidation of the right upper lobe, except the apex. Increased density of the right and left perihilar regions which has begun to resolve at this time. This is the characteristic appearance of Cases I, II, and III.

aggravated and the white blood count was 35,000. An area of dullness with numerous râles appeared in the right apex. He became cyanotic after a severe choking spell and was immediately brought to the hospital (August 2, 1932). He appeared ill and malnourished, weighed 7 pounds 1 ounce, his temperature was 101° F., the white blood count 21,000. On physical examination an expiratory grunt and flaring of the alae nasi were noted. Over the right apex there were medium râles, bronchial breathing, and a high pitched percussion note. The abdomen was slightly distended. The following day a band of dullness was noted in both lungs bordering the spine, more marked on the right. Roentgen examination of the chest revealed consolidation of the right apex and right and left hilar regions, almost identical with the film of Case I taken on the sixteenth day. The shadow on the left was sharper and somewhat more dense than in the two previous cases. The temperature dropped to normal on the following day (sixth day of illness) and remained normal. Respiration was still rapid and the white blood count was 17,000. On the thirteenth day another chest film was taken which showed a decrease in the size of the shadow on the left, while that on the right had increased in area. This increase was all downward, the apex re-

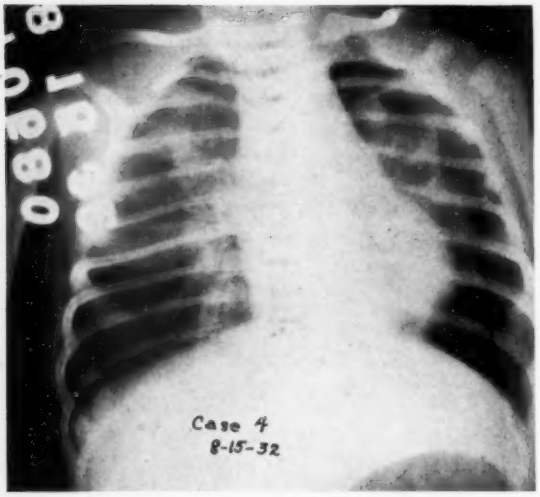

Fig. 3. Case iv. Sixth day of illness. Coarse mottling, confined chiefly to the upper lobes, somewhat more marked on the right. On the original film the right upper lobe appears slightly less dense than in the illustration. This is the characteristic appearance of Cases iv, v, and vi.

maining clear. The baby improved clinically, gaining weight with a good appetite, and the chest signs disappeared. He reacted negatively to 0.01 mg. of tuberculin, and the white blood count was 12,200. Eight months later the baby was seen in the Out Patient Department. He was in apparent good health and the chest was clear to physical examination. Roentgen examination of the chest revealed some remaining

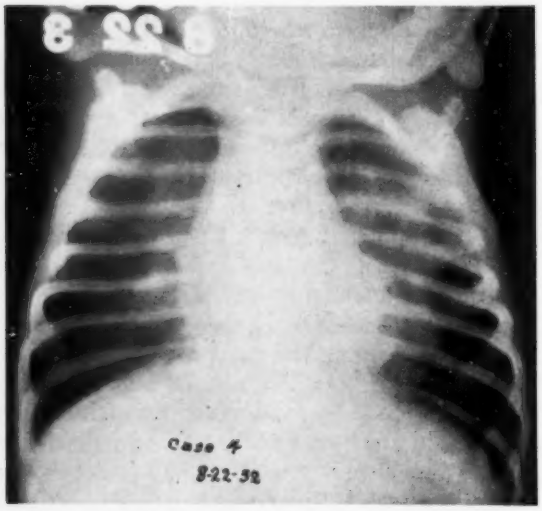

Fig. 4. Case iv. Eleventh day of illness. Beginning resolution at the periphery of the shadow in the right upper lobe. Left essentially unchanged.

increase in the hilar shadows and peribronchial markings to both upper lobes, particularly the right, and a mass of enlarged tracheobronchial lymph nodes in the mediastinum, similar to Case iv (Fig. 5).

Case iv (No. 210580). J. M. C., white female, born June 20, 1932. She was a high forceps delivery, apparently normal after resuscitation by oxygen and weighed 7 pounds 12 ounces. Five days before admission she developed a cough and a temperature of 101° F. "Nose drops" were given five times a day. Dullness and increased breath sounds in the right apex were noted on the third day and the white blood count was 20,500. The following day the child

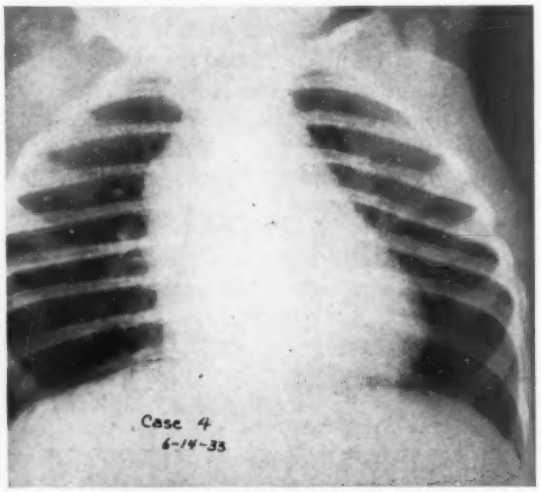

Fig. 5. Case iv. Ten months after onset. Residual shadows in both upper lobes and enlarged tracheobronchial nodes, seen in Cases iii, iv, and vi.

vomited, was breathing irregularly and there was an increase in the size of the dullness with occasional râles. On admission, August 15, 1932, she weighed 9 pounds; temperature was 101.6° F., white blood count 24,150. She was dyspneic and suprasternal retraction was noted. Chest signs were unchanged. A chest film showed increased hilar markings, coarse mottling in the upper two-thirds of both lungs, somewhat more marked on the right. The appearance was similar to the preceding cases, but the shadows were less dense (Fig. 3). There was no reaction to 0.01 mg. of tuberculin injected intradermally. Her condition remained essentially unchanged until the tenth day when the temperature began to fall and no more râles were heard. A roentgenogram three days

later showed definite decrease in the shadows, the periphery of the right lung was fairly clear (Fig. 4). On the fifteenth day there was again no reaction to 0.1 mg. of tuberculin, and the child was much improved. Her weight increased slowly and the temperature remained at 99° F. She was discharged four days later. In two weeks she had gained nearly 2 pounds; her temperature was 99.4° F., and she still had an occasional cough. Roentgen examination revealed a marked clearing of the lung fields, but there were still small areas of increased density in both upper lobes and a mass of enlarged tracheobronchial nodes were present. Films taken at four, six, and ten months show a gradual decrease in the lung shadows, the size of the mediastinal glands remaining relatively unchanged (Fig. 5).

Case v (No. 211123). M. L. B., white female, born June 15, 1932. She was a normal, full term baby, weighing 6 pounds 9 ounces, and was well until August 18 when she vomited one feeding. The following day her temperature was 101° F., and there were high pitched breath sounds in the right apex and axilla with slight dullness, but no râles. The next day she vomited all her feedings, developed a cough, and had a white blood count of 16,200. The temperature remained the same. The fourth day she seemed to improve. A chest film on the twelfth day showed coarse mottling in the upper portions of both lung fields, more on the right, the appearance being very similar to Case iv (Fig. 3). Three days later the dullness in the right apex increased; there was no reaction to 0.01 mg. of tuberculin. The child improved rapidly, was discharged September 6, and was not seen again.

Case vi (No. 211776). D. L. W., white female, born July 1, 1932. She was a small, full term baby, delivered by means of forceps, weighing 4 pounds 7 ounces, apparently normal after birth. On August 30 she developed a cough, vomited, and had a temperature of 101° F. Two days later dullness was noted in the left and high pitched breath sounds in the right axilla with râles in both areas. The temperature ranged between 100 and 101° F. until the seventh day when it was normal. There was little change in her condition on the twenty-first day when a chest film was taken. This showed the same mottling in the upper lobes as the two previous cases. Two months later she was well clinically, and a roentgenogram of the chest showed little change on the right, some decrease of the shadows on the left, and a mass of enlarged glands in the mediastinum. These were not as prominent as in Cases iii and iv. Monthly check up films showed a gradual decrease of the lung shadows, the mediastinum remaining relatively unchanged in appearance. At ten months the child reacted negatively to 0.01 mg. of tuberculin.

Discussion

The roentgen findings may be briefly summarized as follows: Case ii, seen within the first twenty-four hours, showed a marked, diffuse, fine mottling throughout both lungs, characteristic of bronchopneumonia (Fig. 1). On the eleventh day there was consolidation of almost the entire upper right lobe, only the apex remaining clear. The entire left perihilar region and the same area on the right below the consolidation were increased in density. These shadows had a fairly sharp border beyond which the lung appeared normal. Eight days later the consolidation on the left had decreased, chiefly the outer portion, while the shadow on the right was unchanged (Fig. 2). Two other cases, i and iii, were almost identical in appearance on the sixteenth and fifth days, respectively. The films of the last 3 infants showed coarse mottling confined chiefly to the upper lobes, more marked on the right, but no extensive homogeneous shadow as in the first three.

There was a slow but steady resolution of the lung changes in all cases (as in Figs. 3, 4 and 5). This resolution began at the periphery and in eight to ten months only a few small shadows remained (Fig. 5). Vogt[9] has followed a similar case two and one-half years at which time some of the original process still remained.

The development of markedly enlarged tracheobronchial nodes (Fig. 5) in the 3 cases which were followed six weeks or longer is of special interest as glands of this size are usually associated with tuberculosis. However, tuberculosis was ruled out in these cases by repeatedly negative tuberculin tests.

There is no adequate proof that these babies suffered from lipoid pneumonia as they all recovered. However, they have much in common with the published cases of this condition; in view of the exposure to oil inhalation, they were thought clinically to be cases of inhalation pneumonia. The similarity of the pneumonic process to tuberculosis should put one on his guard when interpreting roentgenograms of infants with pulmonary lesions.

SUMMARY

1. A brief discussion of tuberculosis and chronic pneumonia not of tuberculous origin is presented.

2. Six cases of the latter in infants under three months of age are reported with clinical and roentgen findings.

3. The pneumonia which developed in these infants persisted for many months, resolved slowly, and was associated with the development of mediastinal lymphadenitis. The tuberculin test was persistently negative.

4. Although not definitely proved, the diagnosis was thought to be lipoid pneumonia in view of the exposure to oil inhalation and that they have much in common with recorded cases of this condition. Increased knowledge will probably lead to the diagnosis of lipoid pneumonia in many infants with chronic pneumonia.

5. The similarity to tuberculosis is noted, and this should put one on guard when interpreting roentgenograms of infants with pulmonary lesions.

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Vol. 36, No. 6

ACCESSORY ARTICULAR PROCESSES IN THE LUMBAR SPINE*

A REVIEW OF 40 CASES

By HARRY L. FARMER, M.D.
CLEVELAND, OHIO

ONE might conclude from the paucity of literature on accessory articular processes in the lumbar spine that these anomalies are extremely rare, but our experience has been that when roentgenograms of the spine are studied carefully in detail, they are encountered quite frequently.

In 1931, Reisner[6] described one case of accessory inferior articular process in the lumbar spine. Grashey, in a discussion of this case, stated that he had observed nontraumatic fissures through articular processes on several occasions. In 1931 Müller[3] also reported a case of fissure formation of the spinous process of the second lumbar vertebra. In 1932, he[4] reported another case of complete absence of the articular processes of the second lumbar vertebra which he thought might be a more extreme manifestation of the same fundamental disturbance.

Litten,[2] in 1932, described 2 cases of accessory inferior articular processes and 1 case with an accessory superior articular process in the third lumbar vertebra. Rendich and Westing[7] reported 5 cases of accessory inferior articular processes in 1933, and 7 cases were recorded the same year by Nichols and Shiflett.[5] Fulton and Kalbfleisch[1] reported 2 cases in 1934.

All the reported instances of this anomaly have been observed in the inferior processes of the second or third lumbar vertebrae, except the one case cited by Litten of a superior articular process in the third lumbar vertebra. None has been observed in the first, fourth, or fifth lumbar vertebra.

Even to date there are no anatomic specimens of these anomalies. Willis[9] did not mention them in his discussion of vertebral anomalies and according to a recent personal communication has never encountered them. However, this may be readily explained by the fact that these tiny bones are lost in the process of maceration and preparation of the skeletons.

These anomalies are of more than mere academic interest. In instances in which liability or compensation for injury is involved, they are important in differential diagnosis. If compensation is involved, mistaking them for an old ununited fracture may bring about real injustice.

Certainly no one with experience could mistake one of these accessory ossicles for a recent fracture. The bones vary extremely in size and shape. They may be triangular and measure 3 to 4 mm. on each side, or they may be as large as 1×1×1.5 cm. The adjacent articular surfaces on each side of the line of division are smooth and of the density of cortical bone. There are no signs of callus formation. The edges of the adjacent surfaces are rounded and have the same typical appearance of accessory bones found elsewhere, such as at the tip of the acromion, or at the upper outer quadrant of the patella. In more than 50 per cent of the cases in this series (Table 1) the history of injury was so recent that the edges of a fracture could not have been thus rounded and smooth. The line of division may run in an oblique direction, but is more often transverse. When the condition is uni-

TABLE I

TIME ELAPSED SINCE INJURY

	Number of Cases
No injury	1
3 weeks or less	15
3 weeks to 3 months	8
3 months to 1 year	6
1 year to 15 years	10

* From the group of Drs. Hill, Thomas, Farmer and Sackett.

Fig. 1. Large accessory left inferior articular process with combined length of processes on left side greater than on the right. Asymmetry of posterior arch of vertebra below and depression to accommodate for the accessory bone.

lateral, it will be noticed that the total length over all, including the accessory process, is greater than that of the corresponding articular process on the other side. If the accessory process is of large size, there is a depression in the articulation of the vertebra below to accommodate for it (Fig. 1). These findings are incompatible with old fracture. Furthermore, isolated fractures of inferior articular processes occur with extreme rarity.

Congenital divisions in the inferior articulations of the lumbar vertebrae have been observed and recorded as such by my associates and myself since the year 1928. Before that time, a diagnosis of old fracture was made in these cases because we hesitated to call them anomalies without anatomic proof to support such a belief. By 1928, however, we had become so strongly convinced that these divided articular processes were congenital aberrations, that we began to report them as such.

Dr. M. A. Thomas called attention to this condition in a paper on anomalies and variations in the osseous system, read before the Cleveland Medical Arts Club in October, 1927, and he also reported a group of cases before the Industrial and Orthopedic Section of the Cleveland Academy of Medicine in December, 1929.

Table II

Year	Spinal Examinations	Accessory Processes Inferior	Superior
1930	454	5	1
1931	415	5	–
1932	372	4	–
1933	435	6	1
1934	345	6	–
1935	307	7	1
1936	217	4	–
Total	2,535	37	3

Fig. 2. Oblique view showing bilateral inferior processes of the third lumbar vertebra.

Since January, 1930, we have observed 40 patients (Table II) with accessory articular processes of the lumbar spine. Three of these had accessory superior articular processes and the remainder displayed accessory inferior articulating processes

TABLE III

SITE OF ACCESSORY ARTICULAR PROCESSES IN THE LUMBAR SPINE

Site	Inferior	Superior
First	3	–
Second	19	–
Third	25	–
Fourth	7	3
Fifth	1	2

(Table III). This series of cases was collected from a total of 2,535 roentgen examinations of spines. This makes the observed incidence of occurrence of accessory inferior articular processes in roentgenograms of the spine approximately 1.5 per cent. Time no doubt will show this incidence to be low, since more and more of these smaller bones will be discovered as technique is improved and attention is focused on these anomalies.

FIG. 3. Lateral view showing left inferior articular process of the second lumbar vertebra.

FIG. 4. Accessory superior articulating process of the third lumbar vertebra, discovered in routine examination of the genitourinary tract. No history of injury.

There is no doubt that stereoscopic views of the spine enable one to find more of these anomalies. They may be demonstrated in oblique and lateral projections of the spine (Figs. 2 and 3) but are more clearly visualized in the anteroposterior views. The smaller accessory bones can be visualized only in heavily exposed roentgenograms. They may escape detection in lighter exposures which are sufficiently heavy for other diagnostic purposes. We have observed accessory articular processes in numerous instances in the course of examinations of the urinary tract. These are not included in this series of cases.

The roentgenogram from one of these cases is shown in Figure 4, because the

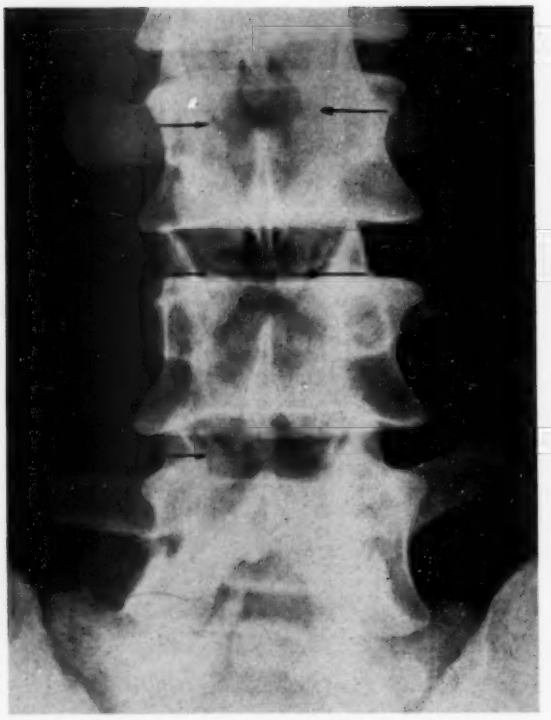

Fig. 5. Bilateral accessory inferior articulating processes on the second and on the third lumbar and unilateral on the right side of the fourth lumbar vertebra. Total of five accessory ossicles in one individual.

Fig. 6. Accessory inferior process on the left side of the first lumbar vertebra. Also a division of the inferior process on the left side of the second lumbar vertebra.

Fig. 7. Bilateral accessory inferior processes of the fourth lumbar vertebra.

Fig. 8. Accessory inferior process on the right side of the fifth lumbar vertebra.

accessory ossicle is in the superior process of the third lumbar vertebra. The patient, a woman, aged thirty-eight, had had urinary symptoms suggestive of calculi. There was no history of injury. The spinal anomaly was discovered in making a roentgenologic examination of the kidneys, ureters and bladder. This case is not included among the three with accessory superior processes mentioned above.

Of the 40 patients with this spinal anomaly, a number exhibited bilateral or multiple accessory processes (Fig. 5). Hence the total number of these small ossicles in the series was 60. There were 11 patients in whom these accessory processes were bilateral. Nine of these were inferior processes and 2 superior processes. All but 2 of the patients in the series were men, but this should not be regarded as significant, because the ratio of men to women among the patients subjected to examination was correspondingly high.

In all the cases heretofore reported in the literature, no instances of this anomaly have been recorded in the first, fourth or fifth lumbar vertebrae. This series contains 3 instances in the first, 10 in the fourth, and 3 in the fifth (Figs. 6, 7 and 8), although the preponderant number of cases were in the second and third lumbar vertebrae (Table III).

Old fractures of the spine were disclosed in only 9 of the 40 cases, and in only 1 was there a recent fracture (Table IV). Other anomalies were noted in 12 cases in the series. Five patients also showed severe arthritic changes in the spine.

TABLE IV

ACCOMPANYING ROENTGENOGRAPHIC FINDINGS

	Number of Cases
Accessory articular processes	40
Other anomalies of spine	12
Old fractures	9
Recent fracture	1
Severe arthritic changes	5

This series of 40 cases of congenital anomalous accessory articular processes of the lumbar spine serves to indicate:

(1) That this finding is much more prevalent than has generally been supposed.

(2) That the anomaly may appear in any of the lumbar vertebrae, in the superior as well as the inferior processes.

(3) That it may be bilateral or multiple.

(4) That it may or may not accompany other structural anomalies.

(5) That it has no relation to injury.

(6) That it is not productive of pain or other symptoms.

(7) That the possibility of this anomaly needs to be kept in mind by the roentgenologist, lest false interpretations be made in cases of injury in which a question of compensation or liability is involved.

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THE ROENTGEN DIAGNOSIS OF OSTEOCHONDRITIS DEFORMANS VERTEBRAE

By EDWARD L. VOKE, A.B., M.D.

Roentgenologist to Peoples Hospital, Akron, Ohio, and Citizens Hospital, Barberton, Ohio.

THE nomenclature used by various authors in describing bone diseases is not uniform, and constant confusion is encountered when attempts are made to classify roentgenographic findings in these conditions. This is particularly true in dealing with the rarer bone lesions which are so often reported in the foreign journals. Many of these lesions are overlooked by the roentgenologist unless he is able to classify his findings into definite groups of disease entities, and this, in turn, becomes simplified when the diseases are given descriptive names. This paper will be limited to one condition found in the juvenile and adolescent spine, which we are pleased to call "osteochondritis deformans vertebrae." This name seems to describe the condition found in Scheuermann's disease and Calvé's disease, together with the variants of these two diseases, which have been given a wide variation of description and classification. Osteochondritis deformans vertebrae is the vertebral manifestation of Legg-Calvé-Perthes' disease in the head of the femur, Osgood-Schlatter's disease in the tibial tubercle, Köhler's disease in the tarsal scaphoid, and many others. All these diseases should be called "osteochondritis deformans." Osteochondritis deformans vertebrae has been given a great variety of names, a few of which are: juvenile kyphosis, vertebral osteochondritis, adolescent kyphoscoliosis, vertebral epiphysitis, osteochondritis dorsalis juvenilis, and kyphosis adolescentium. Harbin and Zollinger[10] have listed many other synonyms in addition to these and were the first to attempt a simplification of terminology.

SUMMARY OF THE DEVELOPMENT OF THE VERTEBRAE

The vertebrae have three centers of ossification, the body and the left and right arches. Union of these centers occurs between the third and eighth year. After this union takes place, outgrowth depends on epiphyseal ossification. Between the ages of eleven and fourteen, an epiphyseal ring forms at the articular margins of each body. These appear on the roentgenogram as triangular shadows, above and below each vertebra. Subsequently, this ring thins out anteriorly and thickens posteriorly, so that a fine line shows above and below each body. This ring remains separated from the body until the age of twenty-one to twenty-five years. Fusion then takes place and length growth is terminated. Schmorl[3] objects to the term "epiphyseal ring" and insists that it should be called the "ossification ring." He maintains that the ring remains intact after the enchondral growth is completed, and that it remains as the marginal ridge which serves as a fixation for the intervertebral disc.

CLASSIFICATION

It is therefore evident that two separate age groups are necessary for classification: the juvenile type, involving the primary centers of ossification, and the adolescent type, involving the secondary centers of ossification. The adolescent type is usually referred to as "Scheuermann's disease" and most of the reported cases fall into this group. The juvenile type is often known as Calvé's disease. Buchman calls this type the true "osteochondritis" and he refers to the adolescent type as "vertebral epiphysitis." Boorstein[2] and others reverse this nomenclature and report cases of osteochondritis in adolescents.

Juvenile Type. The roentgen findings in the juvenile type of osteochondritis deformans vertebrae are well described by Calvé.[4] The earliest finding is the slight narrowing of the intervertebral disc.

Within a few weeks, changes in the vertebral body occur which progresses rapidly. The affected bodies become flattened and their diameter increases. The articular margins are irregular but the intervertebral spaces are preserved. Subsequently, the bodies become "mashed," often more anteriorly than posteriorly. The characteristic wedge deformity is sometimes seen but Calvé's cases were uniformly flattened, and the name "vertebra plana" is used frequently. Federschmidt[9] believes that the vertebral body becomes soft and that the uniform flattening is pathognomonic. The intervertebral disc remains "as high as normal or possibly a little higher." Menard[14] has noted the reconstruction process in the vertebral body and considers this regeneration a characteristic sign. Allende[1] reports a case recently occurring in a child of three. The original diagnosis was tuberculosis, but the bodies of the vertebrae regenerated completely in twelve months and no deformity resulted. Löhr[11] made a search of the literature in 1933 and found a total of 12 cases. He adds the thirteenth case to the series, found in a girl of eight. Regeneration of the flattened vertebrae was observed and a lack of "reactive bone proliferation" was noted in the later films. Brailsford[3] separates the condition into two groups: one showing uniform compression of the body which is classified as vertebra plana; the second group with biconcave bodies, which he calls juvenile osteoporosis. True, many of the cases do simulate senile osteoporosis at one stage but this appearance is explained by the fact that the vertebral body weakens rapidly and the pressure of the disc and the nucleus pulposus causes such a deformity. Further, an osteoporosis does not usually regenerate rapidly and invariably involves other regions of the skeleton. Biconcave vertebrae can be seen in any condition where the cancellous bone structures are softened, thus yielding to the pressure of the nucleus pulposus. This finding has been described in osteomalacia, osteogenesis imperfecta, osteitis fibrosa cystica, Paget's disease, and in metastatic malignancy. These conditions can usually be ruled out by careful roentgenographic study of the skeleton. Osteochondritis is usually limited to one structure and lesions in the spine seem to be confined to that region.

Adolescent Type. The roentgen findings in the adolescent type of osteochondritis deformans vertebrae are well described by Scheuermann.[12] His classical case was a boy fifteen years of age complaining of low back pain and showing a well-marked dorsal kyphosis. The dorsal vertebral bodies were distinctly wedge-shaped and "narrower in front." Three or more bodies are usually involved. The epiphyseal disc was broad and irregular. The contours of the epiphysis were blurred and indistinct and their outlines were irregular and fragmented. Thus, he points out, a disturbance in epiphyseal growth is taking place; normal ossification is being interrupted. Next, the intervertebral spaces become irregular and mottled, and the adjacent vertebral borders are indistinctly outlined. The interspaces gradually become a confused mass and it is difficult to differentiate between the spaces and the bodies.

Regression may begin immediately if proper treatment is instituted and the vertebral outlines gradually resume their definition, although the margins are still irregular. The epiphyses now become differentiated and appear as dense shadows, although not returning to normal size. The vertebral bodies often remain wedge-shaped and the kyphosis will then persist, but neither of these findings is constant. Eckardt[8] describes a case in a boy of fourteen showing involvement of the tenth, eleventh and twelfth dorsal and the third and fourth lumbar vertebrae without wedge deformity or kyphosis. The findings were "cloudy shadowing of the marginal ridges" together with slight narrowing of the intervertebral spaces. Later the borders of the affected bodies were indistinct and jagged. Eventually, there was regression of these findings. Wölfer[15] believes the vertebral bodies become atrophic and are

Fig. 1. Osteochondritis deformans vertebrae, juvenile type.

therefore more permeable to roentgen rays than normal. He reports a case in a girl, aged fifteen, with a kyphosis of the lower dorsal spine, centering on the tenth dorsal vertebra. He contends that Scheuermann's disease alone involves this region and that congenital hunchback, flaccid hunchback and rickets always cause a much higher kyphosis, centering about the fifth dorsal vertebra.

Mau[14] summarizes the pathology in three periods: The period of irritation, the period of destruction and the period of reparation. In the early stages, the epiphyseal plate is first involved. It appears rarefied and its outlines are frayed and motheaten. This accounts for the roentgen findings in the intervertebral spaces, such as irregularity and mottling. During the stage of destruction it becomes difficult to identify the bodies and interspaces. The lateral view especially shows this disordered arrangement. The period of reparation shows the vertebral outlines more distinct and the epiphysis becomes recognizable. At the conclusion of the growing age, the stage of ossification is ended and the progress of the deformity is checked. If the case is diagnosed early and immobilization and rest can be maintained, very little deformity will result.

This same pathological process may involve the nucleus pulposus and the resulting manifestations can usually be found. Schmorl has described these changes as due to overstretching of the cartilage plates in young persons. Damage to these plates leads to enchondral growth, which appears

Fig. 2. Osteochondritis deformans vertebrae, adolescent type.

to burrow into the cancellous structure of the body. These nodular protrusions of cartilage are called Schmorl's nodes and are really a prolapse of the nucleus pulposus. These nodes appear as indentations in the articular borders of the bodies and may burrow deeply into the center of the body. Later, calcification occurs around the border of the node and often the entire node calcifies. Schmorl's nodes have been visible in every adolescent osteochondritis where a thorough search has been made. Schmorl has reported the presence of these nodes in 35 per cent of 3,000 routine examinations and their presence is therefore not pathognomonic.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis must rule out such diseases as tuberculosis, rickets, osteomyelitis, blood dyscrasias, bone tumors, osteomalacia, osteogenesis imperfecta, osteitis fibrosa cystica and syphilis. Many of these conditions are multiple lesions and roentgenograms of the skeleton are invaluable for determining this point. Osteochondritis curiously limits itself to a single region and few cases have been reported where the vertebrae and some other region simultaneously presented epiphyseal changes. Scheuermann[13] has recently found a well-defined case of osteochondritis deformans vertebrae which also shows bilateral epiphyseal deformities at the proximal ends of the tibiae. The age group is another important point. Patients between the age of three and twenty-one include all of the so-called active cases but the healed

Fig. 3. Same patient as in Figure 2, fourteen months later.

Fig. 4. Osteochondritis deformans vertebrae, early adolescent type.

Fig. 5. Same patient as in Figure 4, four months later.

deformities will, of course, persist throughout a lifetime.

Blood dyscrasias, rickets, osteomalacia, osteogenesis imperfecta, and osteitis fibrosa cystica are usually multiple and the roentgen findings are more pronounced in regions other than the spine. Syphilis might lead to confusion but the clinical picture and serological findings are most helpful in ruling out this condition. Bone tumors in the spine of young persons are rare. One vertebral body is most likely to be affected, whereas in osteochondritis the adjacent bodies all show involvement. The same can be said for osteomyelitis, although the clinical picture of infection is usually well defined.

It is evident that our problem of differential diagnosis concerns tuberculosis more than the other diseases mentioned and to rule out an early tuberculous infection is often difficult. Brailsford[3] describes a dense paravertebral shadow, which is visible in the anteroposterior view and closely resembles a paravertebral abscess without the characteristic bulge. Frequent reexaminations fail to show an increase in the size of the shadow, but in tuberculosis the progressive increase in size is well known. Generally, the tuberculous infection is characterized by its destruction of the vertebral body and the consequent necrosis and collapse of the cancellous bone. The interspace adjacent to this focus is completely obliterated but beyond this area, no epiphyseal changes are found. The most important differential point is the bone proliferation which usually takes place following the onset of a tuberculous infection. This is never seen in osteochondritis and the regeneration takes place without new bone production. The healing process shows a more orderly arrangement in osteochondritis. Frequent repetition of the roentgen examination is the only means of making an intelligent differential diagnosis.

CASE REPORTS

Case I. Male, white, aged nine, complained of intermittent back pain which extended up into the neck. Wassermann reaction was negative and no changes were found in the blood picture. Long bones showed no roentgenographic changes. Lateral views of the dorsolumbar spine, July, 1935, showed all the vertebral bodies to be flattened and markedly decalcified except at the articular margins (Fig. 1). The appearance of malacia in the individual bodies simulates Köhler's disease in the navicular bone of the foot. The child was placed in a brace and the spine was immobilized. After one year, all symptoms have disappeared and the roentgen report in August, 1936, from another city states: "The bodies of all the vertebrae have almost completely regenerated and are of normal density."

This case demonstrates the juvenile type of osteochondritis deformans vertebrae.

Case II. White male, aged eighteen, complained of indefinite back pain of one year's

duration without history of trauma. He has gradually become "round shouldered." Laboratory tests were negative. Lateral view of the dorsal spine taken May, 1934, shows kyphosis, fragmentation of the vertebral margins, wedge deformity of the bodies and Schmorl's nodes (Fig. 2). Loss of density is seen within the vertebral bodies. The patient was placed in a body cast and fourteen months later the spine was re-examined (Fig. 3). The kyphosis persists but the fragmentation is disappearing. The wedge deformity is still visible. There is marked regeneration of the vertebral margins. The patient is now apparently normal and has no complaints except that he is slightly "stoop shouldered."

This case demonstrates the adolescent type of osteochondritis deformans vertebrae which had already progressed to the deformity stage before correct diagnosis and treatment could be instituted.

Case III. White male, aged sixteen, football player with probable injury. Complained of severe back pain of two months' duration. Patient was large for his age and dorsal kyphosis was easily noticed. Lateral dorsal spine shows irregularity and fragmentation of all the vertebral margins. Bodies show slight flattening and beginning wedge deformity but interspaces are preserved (Fig. 4). Patient was placed in plaster shell with absolute rest in bed. Four months later, the symptoms had subsided and the cast was removed. Re-examination of the dorsal spine shows regeneration of bodies and reduction of fragmentation. Kyphosis has almost disappeared (Fig. 5). The lumbar spine shows a well-defined Schmorl's node at the superior border of the fourth lumbar vertebra (Fig. 6).

This case illustrates the effect of early treatment on a moderately advanced case of osteochondritis deformans vertebrae.

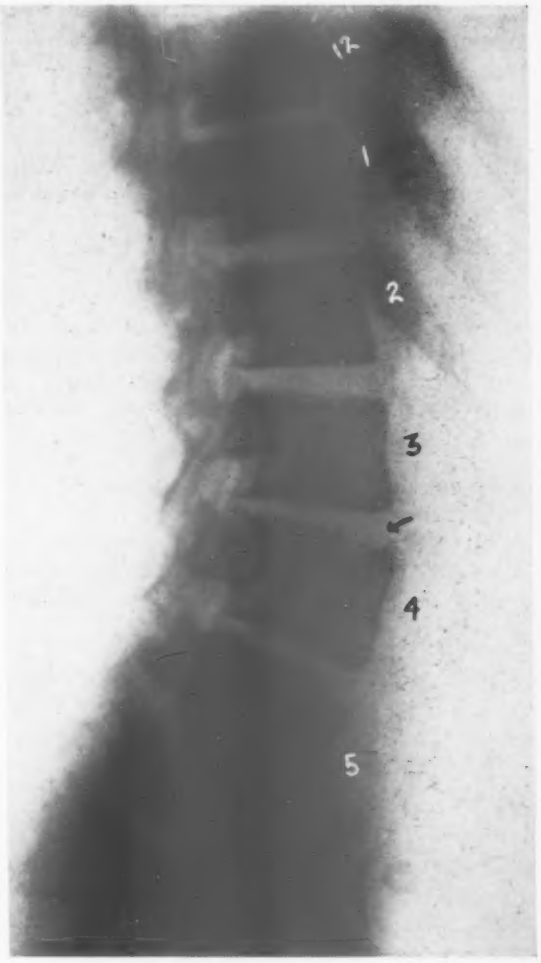

Fig. 6. Lumbar spine showing Schmorl's node at superior border of fourth lumbar vertebra.

SUMMARY

The positive roentgen findings in the juvenile type of osteochondritis deformans vertebrae are:

1. Flattening of the vertebral body.
2. Preservation of the intervertebral space.
3. Increased transverse diameter of the body.
4. Irregularity and fragmentation of the borders of the body.
5. Decreased density of the body.
6. Regeneration of the body without bone proliferation.

The positive roentgen findings in the adolescent type of osteochondritis deformans vertebrae are:

1. Kyphosis.
2. Increased density of the vertebral borders with fragmentation in the more advanced cases.
3. Area of diminished density within the body.
4. Slight flattening of the body.
5. Preservation of the intervertebral

space early but encroachment later when deformity of the body advances.

6. Wedge deformity of the body.

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VOL. 36, NO. 6

MULTIPLE TUMORS WITHIN THE SPINAL CANAL

DIAGNOSIS BY MEANS OF LIPIODOL INJECTED INTO THE SUBARACHNOID SPACE (MYELOGRAPHY)

By JOHN D. CAMP, M.D.
Section on Roentgenology, The Mayo Clinic
ROCHESTER, MINNESOTA

THE method of injecting a radiopaque oil (lipiodol) into the subarachnoid space as a means of localizing tumors within the spinal canal was introduced by Sicard and Forestier in 1922. They recommended that 2 c.c. of lipiodol be injected into the basal cistern or into the lumbar space, preferably the former; they depended on obstruction of the radiopaque oil by the lesion for its localization. This technique is not without its disadvantages, because such small amounts of oil tend to separate into globules of various sizes which easily pass a nonobstructing tumor without revealing its presence. Also when 2 c.c. of oil is distributed along the subarachnoid space, pseudo arrests which simulate a partially obstructing lesion are not uncommon. Since greater success in the treatment of tumors within the spinal canal can be obtained the earlier the lesion is diagnosed, I felt that larger amounts of oil were indicated in order to completely fill the subarachnoid space at any desired level and to reveal the tumor by virtue of its filling defect, before obstruction has occurred. This opinion is also supported by Odin, Rumström and Lindblom. For several years past I have advocated the use of at least 5 c.c. of radiopaque oil in the subarachnoid space, and have stressed the necessity for a thorough study of the excursion of the oil, with the patient in the prone, supine, oblique and lateral positions on a tilting roentgenoscopic table.[1] The success of this procedure is evidenced by the fact that in this manner numerous nonobstructing and partially obstructing tumors have been identified, many of which were associated with the observation of a normal spinal fluid. Further proof of the efficiency of this technique is emphasized by the facts that, during the last five years at The Mayo Clinic, this method of examination has been used with increasing frequency, the number of tumors of the spinal cord that have been localized and successfully operated on has increased each year, and during this time the average size of the tumor found at operation has been smaller than that of tumors previously observed.

It is recognized that there is a small element of risk in this procedure, and that the oil is not devoid of irritating properties. However, it is not used or recommended when a lesion can be accurately diagnosed or localized by other clinical or roentgenologic methods. When the procedure is indicated, it is felt that the advantages derived from its use far outweigh the element of risk.

By a careful study of the shape of the shadow cast by the oil and of the nature of the defect observed, it usually is easy to determine whether a tumor is extradural subdural, or intramedullary, and frequently the position of the tumor as related to the anterior, posterior or lateral aspects of the cord can be elicited. These points, of course, may be of great import in predicting the nature of the tumor, particularly in the case of a protruded intervertebral disc.

The majority of tumors of the spinal cord are single and, as far as I am aware, no case of multiple tumors diagnosed preoperatively by myelography has been reported in the literature. Multiple tumors may produce confusing clinical signs, and unless they are recognized before operation, the surgical results may prove disappointing since if the lesions are separated by several segments, some may be overlooked. The significant roentgenologic data concerning the following cases of multiple

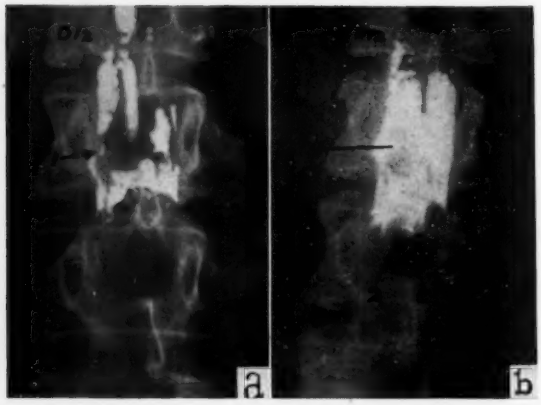

Fig. 1. Case 1. Multiple attached neurofibromas. *a*, Lipiodol arrested at second lumbar vertebra, with sharply outlined defect indicating subdural tumor (2); *b*, film three hours later; lipiodol accumulated above tumor (2). Within the oil-shadow opposite the first lumbar vertebra can be seen the defect of another subdural mass (1) representing a second tumor. The third tumor is not revealed because of complete obstruction produced by the middle tumor.

tumors are presented since they emphasize the value of myelography in anticipating the surgical approach to such lesions. In each case, except in Case II, the diagnosis of multiple tumors or lesions was made by the roentgenologist before operation.

REPORT OF CASES

Case 1. *Multiple neurofibromas.* A woman, aged forty-five, complained of pain of a year's duration in the legs and back. The pains were sharp and shooting and extended down the thighs. These pains ordinarily were worse at night, but for three weeks prior to examination at The Clinic they were present constantly.

Physical and neurologic examination were negative except that extreme tenderness was present over the sacroiliac regions. The cerebrospinal fluid was yellow and there was evidence of complete block. Because the exact level of the suspected tumor could not be determined by clinical methods, myelography was advised. In order to be sure that the oil was introduced above the lesion, 5 c.c. of lipiodol was injected into the basal cistern. The excursion of the oil was observed roentgenoscopically as it passed caudad with the head of the patient elevated. Opposite the first lumbar vertebra the oil was arrested, as may be noted in Figure 1*a*. The lower margin of the defect was sharply defined, which indicated that the lesion was subdural. Because the lesion that was revealed roentgenologically was slightly higher than was anticipated by the neurologist, the patient was taken back to her room and kept in a sitting position. This was done because experience in the past has shown that when the patient was kept upright for a few hours after the first examination in cases in which the obstruction at first appeared to be complete, a small portion of the oil might work itself down along and below the lesion and thus define its lower limit. At the end of three hours a second roentgenoscopic study revealed the changes noted in Figure 1*b*. At this time all the oil had gravitated down to the lesion originally observed, and within the mass of oil that had accumulated above it could be seen a well-defined subdural defect indicating

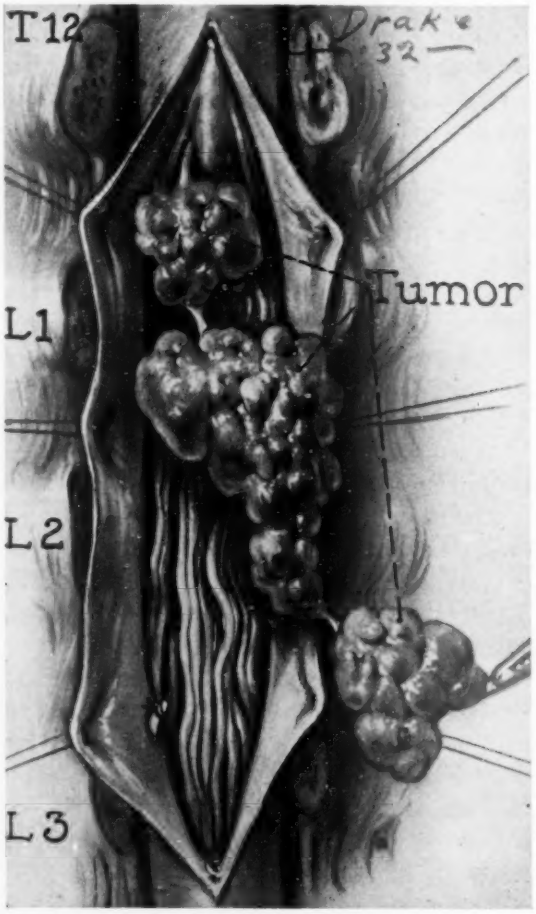

Fig. 2. Case 1. Multiple attached neurofibromas. Drawing representing tumors exposed and partially removed at operation.

a second mass (defect 1, Fig. 1*b*) that was not revealed at the first examination. It was evident, therefore, that an atypical, irregular subdural tumor, or two tumors close together were present.

Laminectomy was performed over the lesion, and three contiguous neurofibromas attached to the second lumbar root were revealed (Fig. 2). The two upper tumors were subdural and corresponded to the two defects noted roentgenographically. The upper tumor was 2.4 cm. in diameter and corresponded to defect 1 indicated in Figure 1*b*. The middle tumor was 1.6 cm. in diameter, and the upper border of this mass, which had produced complete obstruction of the oil, corresponded to defect 2 in Figure 1*a* and *b*. The lower tumor was 1.2 cm. in diameter and was situated extradurally, as may be noted in Figure 2. It was not revealed roentgenologically because passage of the oil was completely obstructed above by the middle tumor. All of these tumors were removed intact, together with the second lumbar root to which they were attached. No other tumors were revealed. The patient made an uneventful recovery and was completely relieved of her symptoms.

CASE II. *Multiple subdural neurofibromas.* A man, aged forty-seven, came to The Clinic in August, 1931, because of pain in the left lower part of the abdomen and numbness of the legs. Three years previously he had experienced a sudden, severe pain in the left loin. The pain had extended around to the front, above the pubis, and was associated with rigidity of the muscles of the abdominal wall. These attacks had lasted for several minutes and had recurred at intervals of about a week. During the preceding year he had had indefinite distress in the lower part of the abdomen most of the time, with exacerbations of pain during the attacks mentioned. At this time he had noticed that coughing and sneezing always provoked an attack. Two months before he came to The Clinic numbness had developed in the left leg, below the knee. Shortly thereafter numbness also developed in the right leg.

Physical and neurologic examinations revealed only that the left leg was spastic and that the Babinski sign was bilaterally positive. Tenderness was diffuse over the abdomen, particularly at the left costovertebral junction. The cerebrospinal fluid was yellow, the test for globulin was positive, and the protein content

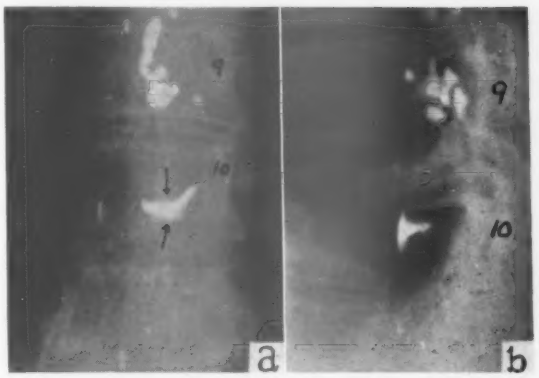

FIG. 3. Case II. Two attached neurofibromas. *a*, Biconcave deformity in mass of lipiodol, opposite tenth thoracic vertebra, produced by inferior border of first subdural tumor and superior border of second subdural tumor; *b*, lateral view; lipiodol outlining upper border of first tumor opposite ninth thoracic vertebra and biconcave mass of lipiodol opposite tenth thoracic vertebra, revealing inferior border of first tumor and superior border of second tumor.

was 1000 mg. per 100 c.c. There was no response to pressure over the jugular veins.

The neurologic diagnosis of a tumor of the spinal cord at the level of the ninth and tenth thoracic vertebrae was made. Myelography was advised for accurate localization of the lesion. Because a complete block of the cerebrospinal fluid was present the surgeon felt that 2 c.c. of lipiodol would be sufficient to localize the obstruction. This was injected into the basal cistern, and when the head of the patient was elevated by the tilting roentgenoscopic table, the oil, which had broken up into globules, was observed to pass slowly caudad in the subarachnoid space. Opposite the ninth thoracic vertebra there was an incomplete obstruction which produced in the shadow cast by the oil, a sharply outlined concave deformity indicative of a subdural tumor (Fig. 3*b*). Some of the oil passed slowly by the obstruction and collected opposite the tenth thoracic vertebra where another sharply defined, concave defect was observed (Fig. 3*a* and *b*). At the time of the examination this was interpreted as the lower border of the tumor. Laminectomy was performed over the ninth, tenth and eleventh thoracic segments, and opposite the ninth and tenth thoracic vertebrae two subdural neurofibromas that were attached by a short pedicle were found and removed. They were on the left side and

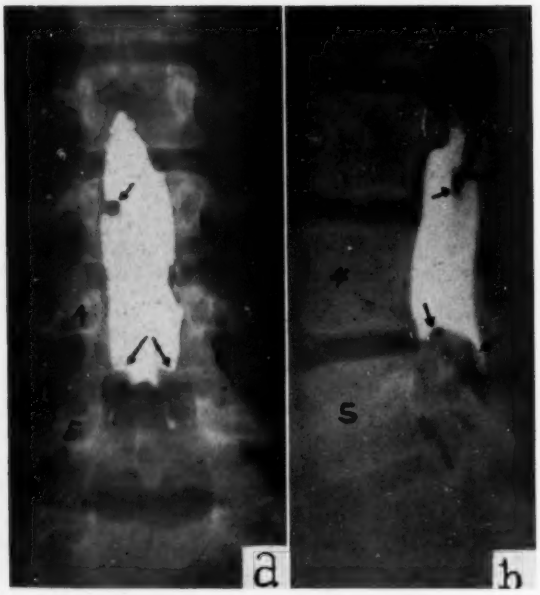

Fig. 4*a* and *b*. Case III. Neurofibromatosis (von Recklinghausen's disease). Multiple subdural defects produced by multiple neurofibromas. Large tumor outlined at upper border of fifth lumbar vertebra.

the upper tumor was attached to the ninth posterior root while the tenth posterior root ran over the tumor. Both roots were cut and the tumors were removed intact. The upper tumor measured 3 by 2 by 1.5 cm., and the lower tumor measured 2 by 1.5 by 1.5 cm. The patient made an uneventful convalescence, and was entirely relieved of his symptoms.

In reviewing the roentgenograms in this case after operation, it was obvious that the upper margin of the upper tumor was represented by the oil defect opposite the ninth thoracic vertebra (Fig. 3*b*) and that the inferior aspect of the upper tumor and the superior aspect of the lower tumor were represented by the biconcave mass of lipiodol opposite the tenth thoracic vertebra (Fig. 3*a* and *b*). If greater attention had been paid to the significant shape of these shadows, a diagnosis of multiple tumors would have been possible before operation.

Case III. *Neurofibromatosis (von Recklinghausen's disease)*. A girl, aged thirteen, complained of pain in the left thigh of three years' duration. The pain was worse at night and was relieved by walking about. Physical examination revealed multiple interesting changes which heretofore had not been observed by the patient or by previous examiners. In both optic discs were hyaloid remnants and in the choroid of the right eye there was a small, tubercle-like lesion. The right ear was deaf even to the sound of a loud voice. The right side of the palate was paralyzed and the right vocal cord was fixed in the midline. The left side of the diaphragm was high, immobile and revealed evidence of left phrenic paralysis. The left knee jerk was slightly diminished. There were no palpable masses in the soft tissues. Lumbar puncture revealed that the cerebrospinal fluid was clear, without evidence of block and that the value for protein was 100 mg. per 100 c.c. Because of uncertainty concerning the situation of the lesion which was producing the pain in the left thigh, myelography was advised. Five cubic centimeters of lipiodol was introduced between the fourth and fifth lumbar vertebrae, and its excursion was observed by means of the roentgenoscope. Abnormalities were noted only in the lumbar region, where the changes observed in Figure 4 (*a* and *b*)

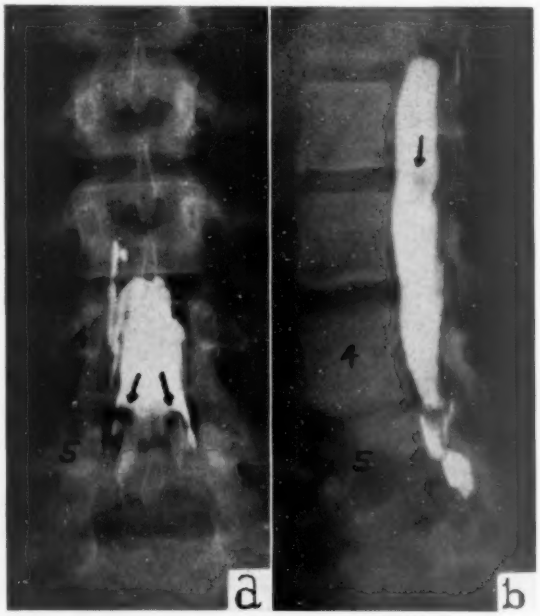

Fig. 5. Case III. Neurofibromatosis (von Recklinghausen's disease). Same case as that represented in Figure 4 after patient had been in sitting position for three hours. Lipiodol has gravitated down about lowermost tumors, better defining their extent. Arrow in lateral view indicates one small tumor.

were noted. It was obvious that multiple subdural masses were present, and in order better to outline the mass opposite the fifth lumbar vertebra, the patient was kept in bed in a sitting position for three hours in order to allow the lipiodol to gravitate down to and about the lower lesion. At the end of that time the changes revealed in Figure 5 (*a* and *b*) were noted. It was obvious that there were multiple small subdural tumors and a large tumor opposite the fifth lumbar vertebra. In view of the other physical findings, von Recklinghausen's disease was suspected.

Laminectomy from the second sacral vertebra to the first lumbar vertebra was performed, and multiple subdural neurofibromas of various sizes, attached to the nerve roots, were revealed. About fifty tumors in all were removed. The largest, which occurred opposite the fifth lumbar vertebra, measured 5 by 3 by 3 cm. in various diameters, and corresponded to the largest mass seen in the roentgenograms (Figs. 4 and 5). It was impossible to remove other numerous very small tumors attached to the nerve roots, but in spite of this the patient made an excellent recovery and was completely relieved of pain. The prognosis, of course, is doubtful since the remaining tumors probably will grow and eventually will provoke symptoms.

Case iv. *Subdural extramedullary meningioma and multiple prolapsed intervertebral discs.* A farmer, aged sixty-nine, came to The Clinic in June, 1936, because of inability to walk. He had been well until three years previously when he had an attack apparently of urinary obstruction. In December, 1934, he had complained of tingling in his right arm, and following a chiropractic treatment for this he had experienced some pain in the left side of his back which had been relieved by exercise and aggravated by lying down. About this time he also had noticed a prickling sensation in both feet. In September, 1935, his legs had become weak; the right leg was weaker than the left, and it was necessary for the man to use a cane for support. The weakness had gradually increased until two months before he came to The Clinic, when he was unable to walk.

Physical examination revealed that the patient was unable to move either leg. Pain, vibration and temperature sense were lost in each leg. There were marked ankle clonus and bilateral positive Babinski signs. On neurologic

Fig. 6. Case iv. Intraspinal protrusion of multiple intervertebral discs associated with subdural meningioma (see also Figure 7). *a*, Anteroposterior view; defects in lipiodol produced by protruded intervertebral discs between second and third, third and fourth and fourth and fifth lumbar vertebrae. Other protrusions not visible in this film; *b*, lateral view; characteristic anterolateral extradural defect attributable to intraspinal protrusion of intervertebral disc between third and fourth lumbar vertebrae. Other protrusions not visible in this film.

examination, the lesion was placed at the level of the tenth and eleventh thoracic vertebrae, but because the lumbar puncture revealed no evidence of a block and because the examination of the cerebrospinal fluid gave negative results, myelography was advised in order definitely to determine whether the underlying process was a tumor (as suspected) or a degenerating lesion.

Five cubic centimeters of lipiodol was introduced into the subarachnoid space in the lumbar region. Roentgenoscopic examination revealed the changes depicted in Figures 6 (*a* and *b*) and 7 (*a* and *b*). The deformities of the shadow cast by the oil opposite each of the intervertebral discs between the lumbosacral junction and the tenth thoracic vertebra, where the oil was completely blocked, were obviously caused by an antero-extradural mass at the level of each intervertebral disc (Fig. 6 *a* and *b*). At the point of obstruction opposite the tenth thoracic vertebra the margins of the

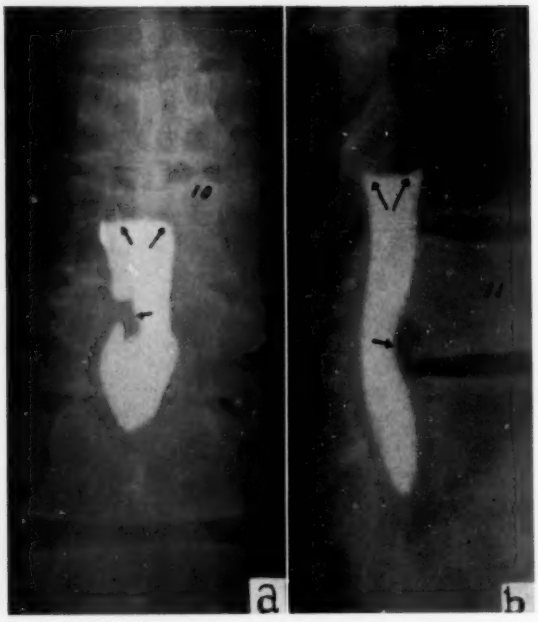

Fig. 7. Case iv. Subdural meningioma associated with intraspinal protrusion of multiple intervertebral discs (see also Figure 6). *a*, Obstruction of lipiodol attributable to subdural meningioma opposite tenth thoracic vertebra and defect of protruded intervertebral disc between tenth and eleventh thoracic vertebrae; *b*, characteristic subdural defect produced by meningioma opposite tenth thoracic vertebra and extradural defect attributable to protruded intervertebral disc between eleventh and twelfth thoracic vertebrae.

column of oil were concave and sharply defined. indicating the presence of a subdural extramedullary mass (Fig. 7*a* and *b*). A roentgenologic diagnosis was made of a subdural extramedullary tumor at the tenth thoracic vertebra and prolapse of each intervertebral disc between the tenth thoracic and first sacral vertebrae. Laminectomy from the ninth to the twelfth thoracic vertebrae was performed. At the level of the tenth thoracic vertebra a subdural extramedullary meningioma, 2 by 2.5 cm. was found and removed. The intervertebral disc between the eleventh and twelfth thoracic vertebrae was extruding into the spinal canal, and a decompressive laminectomy was made over this point. It was deemed inadvisable to extend the laminectomy further. A catheter was passed down the canal posteriorly without meeting obstruction. When a catheter was passed cown the canal anteriorly it met an obstruction opposite the intervertebral disc below. As one extruded disc had been found just below the tumor at the site indicated by the roentgenograms and the catheter was obstructed anteriorly below this point, it was felt that the diagnosis of multiple prolapsed intervertebral discs was substantiated.

Following operation, the patient showed little if any improvement in muscular strength. There was some return of sensation, but vibratory sense was definitely lost.

Case v. *Subdural extramedullary neurofibroma and multiple prolapsed intervertebral discs.* A man, a linotype operator, aged thirty-six, came to The Clinic in March, 1932, because of difficulty in walking. In 1927, following exposure to a draught, he had experienced persistent pains in the right shoulder. In 1929, weakness in the right knee, inability to move the right toes and wasting of the muscles of the right thigh had developed. In 1931, he had had an inguinal hernia repaired under spinal anesthesia. When in the hospital his right leg had become stiff, and partial numbness from the midsternum down had developed. Soon afterward urinary and fecal incontinence had appeared.

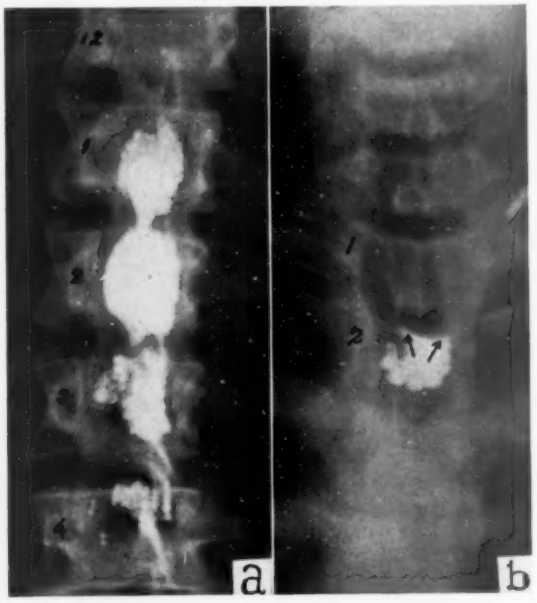

Fig. 8. Case v. Intraspinal protrusion of multiple intervertebral discs associated with subdural neurofibroma. *a*, Defects in shadow of lipiodol produced by protruded intervertebral disc between first and second, second and third, and third and fourth lumbar vertebrae; *b*, lipiodol obstructed by lower border of neurofibroma opposite upper margin of second thoracic vertebra. Sharply defined concave shadow indicates subdural position of tumor.

Physical examination revealed a spastic lower right leg. A bilateral, positive Babinski sign and exaggerated knee jerks were present. The abdominal reflexes were absent, and below a band-like level around the thorax, pain sensation was entirely absent. The Romberg sign was positive. On the basis of neurologic examination, a diagnosis of tumor of the spinal cord at the level of the second thoracic vertebra was made, but because roentgenologically there was some questionable erosion of the pedicles of the twelfth thoracic and first and second lumbar vertebrae, myelography was advised to exclude the possibility of a lesion at this level. Five cubic centimeters of lipiodol was introduced into the lumbar region, and opposite the intervertebral discs, from the first to the fourth lumbar vertebrae, a definite extradural narrowing of the shadow cast by the oil was observed (Fig. 8*a*). Above the first lumbar vertebra the oil moved normally until it reached the second thoracic vertebra where it was completely arrested. At this point there was a sharply defined concave defect in the shadow cast by the oil, which was characteristic of a subdural extramedullary tumor (Fig. 8*b*). Laminectomy was performed over the second thoracic segment and a vascular, subdural neurofibroma, 3.5 by 1.5 cm., which was attached to the second right posterior root, was removed. Following the operation the condition of the patient improved about 50 per cent. In the absence of symptoms referable to the lumbar segments, it was deemed inadvisable to explore the lumbar region over the defects, which may be noted in Figure 8*a*. Although the significance of these defects was not obvious at the time, experience has since shown that defects of this type are almost always characteristic of prolapsed intervertebral discs. The patient has not been heard from since his discharge from the hospital.

COMMENT

In the before-mentioned cases, the importance of studying the entire spinal canal by means of the roentgenoscope, after radiopaque oil has been introduced into the subarachnoid space, has been emphasized, and the value of using an adequate amount of oil (at least 5 c.c.) in revealing nonobstructing lesions has been demonstrated.

If the roentgenologic examination is limited to roentgenograms alone and obstruction only is looked for, many partially obstructing or nonobstructing lesions, some of which may be multiple, may be overlooked. In a recent series of 72 cases in which tumors affecting the spinal cord were localized by means of myelography, in 4 per cent of the cases the lesions were multiple and were so diagnosed by the roentgenologist before operation.

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THE ROENTGENOGRAPHIC DEMONSTRATION OF RUPTURE OF THE INTERVERTEBRAL DISC INTO THE SPINAL CANAL AFTER THE INJECTION OF LIPIODOL*

WITH SPECIAL REFERENCE TO UNILATERAL LUMBAR LESIONS ACCOMPANIED BY LOW BACK PAIN WITH "SCIATIC" RADIATION

By AUBREY O. HAMPTON, M.D.
BOSTON, MASSACHUSETTS
and
J. MAURICE ROBINSON, M.D.
SAN FRANCISCO, CALIFORNIA

THIS paper presents the roentgen findings in a group of 50 patients operated upon at the Massachusetts General Hospital for the relief of symptoms of spinal cord or nerve root compression caused by cartilaginous lesions protruding from the posterior margins of the intervertebral discs. Investigation has shown that these lesions are ruptures of portions of the intervertebral discs into the spinal canal, similar to the posterior protrusions of the nucleus pulposus described by Schmorl, Andrae and others.

The chondromas, enchondromas, ecchondroses, traumatic ruptures of the intervertebral disc, and so forth, of which Mixter and Ayer in 1935 found 47 cases reported in the literature, undoubtedly represent a similar or identical pathologic process. Unlike those cases, however, which almost invariably were associated with the clinical findings of tumor of the spinal cord or cauda equina, the majority of the group under consideration were unilateral ruptures of the lower lumbar discs and they were associated with clinical findings almost indistinguishable from those of low back strain, sacroiliac disease, "sciatica" and related conditions. This clinically interesting series of cases has been the object of considerable study by various members of the staff of the Massachusetts General Hospital and the importance of these lesions as a factor in the production of low back pain is being elucidated. Preliminary papers have already appeared by Mixter and Barr, and Mixter and Ayer.†

This report will stress the value of roentgen examination of the subarachnoid space in these cases after the injection of lipiodol, for this procedure has become of paramount importance in differential diagnosis. By such examination it was possible to demonstrate all but 1 of the 31 ruptures operated upon in the past three years, practically all of which were unilateral ruptures of the fourth or fifth lumbar discs accompanied by low back pain with unilateral radiation down the posterior thigh and leg.

We shall present the technique of and indications for lipiodol examination, the findings on the usual roentgenograms, the correlation of the surgical and roentgen findings, and a study of the basis of the normal roentgen picture after the use of lipiodol. The interpretation of the characteristic defects produced by these lesions will be illustrated by representative cases.

For convenience of discussion the ma-

† Dr. W. J. Mixter, who operated upon nearly all of these patients, and Dr. Joseph Barr are now preparing papers on the neurological, surgical, and orthopedic features of this lumbar group. Their papers should be consulted for a more detailed review of the literature and for a discussion of the clinical, surgical and pathologic aspects, including the end-result studies. We are greatly indebted to them for their kindness in making available to us the clinical material.

* From the Department of Roentgenology of the Massachusetts General Hospital, Boston. Read at the Thirty-seventh Annual Meeting, American Roentgen Ray Society, Cleveland, Ohio, Sept. 29-Oct. 2, 1936.

terial has been divided into two groups: lesions of the cervical and thoracic area (11 cases) and lesions of the lumbar area (39 cases).

CERVICAL AND THORACIC GROUP

These cases will be discussed only briefly, as the majority of chondromas, ecchondroses, etc., reported in the literature were in these areas, and the findings in these cases have been adequately described (Stookey, Elsberg, Mixter and Barr, Mixter and Ayer, and others). Some of these writers have not found roentgen examination in these cases after lipiodol of much value, contrary to the experience at this hospital.

Four of the 8 cervical lesions were studied after the cisternal injection of lipiodol; these showed signs of a partial or complete block. In 2 of these the existence of such a "block" at the level of a narrowed intervertebral space justified the roentgen diagnosis of rupture of the disc into the spinal canal (Figs. 1*b* and *c*). In 2 other cases lipiodol was injected but the examination could not be carried out as the lipiodol could not be dislodged from the cranium.

The routine roentgenograms of the 3 thoracic lesions revealed no significant changes, but in the single case examined after the injection of lipiodol a definite block was noted opposite the disc involved (Fig. 1*c*).

LUMBAR GROUP

Of the 39 lesions in the lumbar area, 36 (92 per cent) were located at L_4 or L_5 disc.* Ruptures were twice as common at L_4, at which level there were 24 ruptures, as at L_5, at which there were 11. One case showed a rupture of more than one disc (L_4 and L_5) and 3 were at other lumbar levels.

In 8 cases the lesion was "bilateral"* and produced the clinical picture of tumor of

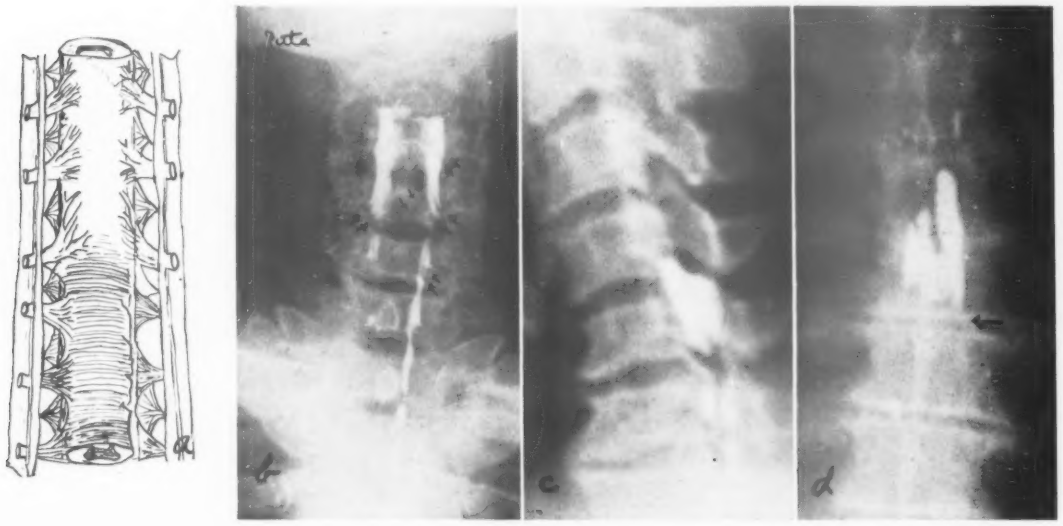

FIG. 1. *a*. Anatomical drawing of the cervical cord (taken from Peiper). *b*. The lipiodol is arrested opposite the intervertebral disc which is ruptured posteriorly. The central band of diminished density is due to normal spinal cord. The nerve roots and radicles are indicated by arrows. *c*. The joint space between the fifth and sixth lumbar vertebra is narrowed. A block is demonstrated at the level of the intervertebral disc. *d*. The descent of lipiodol is arrested at the inferior margin of the seventh dorsal vertebra. There is no "cap" formation.

* The disc number refers to that below the body of the vertebra, e.g., L_4 disc refers to the intervertebral disc between the fourth and fifth lumbar vertebrae. Similarly L_4 nerve root refers to the nerve root leaving the lumbar canal through L_4 intervertebral foramen, which is that between the fourth and fifth lumbar vertebrae. The term "ruptured disc" refers to a posterior rupture of the intervertebral disc. A "bilateral" rupture is a single rupture which extends completely across the midline, producing bilateral involvement.

the cauda equina with definite tumor and sensory disturbances as in the similar chondromas, ruptures of the disc, etc., reported in the literature. Bilateral sciatic pain was an outstanding finding in all of these cases as it is in involvement of the cauda equina from other causes. It is interesting to note in this regard that Goldthwait in 1911 reported 1 case, and Dandy in 1929 reported 2 cases of traumatic rupture of the intervertebral disc with this clinical picture; which led them to suggest that such lesions might be a more common cause of sciatica than was recognized.

Unlike the above lesions, the remaining 31 cases were unilateral, and in this group, as we have said, the chief complaint of the patient was pain in the low back or buttock, radiating down the back or side of one or the other thigh or calf, corresponding to the side on which the lesion was found. Practically all of these cases had been treated as cases of sacroiliac disease or low back strain before the correct diagnosis was made. There was nothing of constant significance in the age, history or relation to trauma which permitted a definite differential diagnosis. Of these factors a history of trauma seemed to bear some relationship as it was present in approximately 60 per cent of the cases.

ROUTINE ROENTGENOGRAMS

In the study of the routine roentgenograms of this group we were particularly interested in the incidence of narrowing of the intervertebral joint space corresponding to the lesion found at operation. Other variations from the normal were also considered. In other words, the attempt was made to determine whether the routine roentgenogram was of value in the localization of the lesion.

No significant changes were noted in 19 of the 39 cases. Of the 20 cases with such changes, 12 were associated with a history of trauma. A history of trauma was obtained, however, in a nearly equal number of these patients without significant changes being present.

Of the 24 lesions at L_4, three showed narrowing of this disc alone, 5 showed narrowing of both L_4 and L_5 disc, and 5 showed narrowing at L_5 alone, with or without generalized changes in the margins of the vertebral bodies. An L_3 lesion showed narrowing locally. The case with L_4 and L_5 rupture had narrowing at both discs.

Of the 11 lesions at L_5 definite local changes were noted in only 5. It will be noted that narrowing of this disc occurred more frequently when the lesion was at L_4 than it did when the lesion was at its own level. It should probably be disregarded in the differential diagnosis, particularly since it is difficult to determine when the L_5 disc is definitely narrowed and since this disc is narrowed in many patients who have no complaints referable to the low back. If this is done greater significance can be given to narrowing of the disc at other interspaces. Thus, disregarding changes at L_5, a decrease in the width of the joint space at L_4 was of localizing value in 25 per cent of all the cases, 33 per cent of L_4 ruptures.

Although narrowing of the vertebral interspace with or without new bone formation is often indicative of rupture of the nucleus pulposus, this finding does not indicate whether the rupture is into the body of the vertebra, the spinal canal or elsewhere. Such narrowing has not therefore been used as an indication for the injection of lipiodol, although it has sometimes been of suggestive value. As we have stated, we have not been interested in the significance of these narrowings except as they affected the diagnosis of posterior rupture of the intervertebral disc, for their presence or absence has not had any definite prognostic significance (Fig. 2*a*, *b*, *c*, *d*, *e*, and *f*).

The absence of consistent narrowing of the intervertebral joint space in the presence of a rupture of the nucleus pulposus may be explained as follows: Schmorl states that, due to the expansile nature of the nucleus pulposus, it tends to maintain

its size unless there is appreciable loss of substance, e.g., he points to the familiar picture of osteomalacia, where there is an increase in size of the nucleus producing the so-called "fish bone vertebrae." Barr has called attention to the fact that the size of the protruding portion of the ruptured disc is quite small compared to the total mass of the disc. In this series of cases, however, there was no definite relation between the size of the rupture and the degree of narrowing of the disc.

Degenerative changes about the margins of the lumbar vertebrae in this group of cases were consistent with the age of the patient. The majority of our patients were young adult males ranging in age from twenty to forty-five, in contrast to the

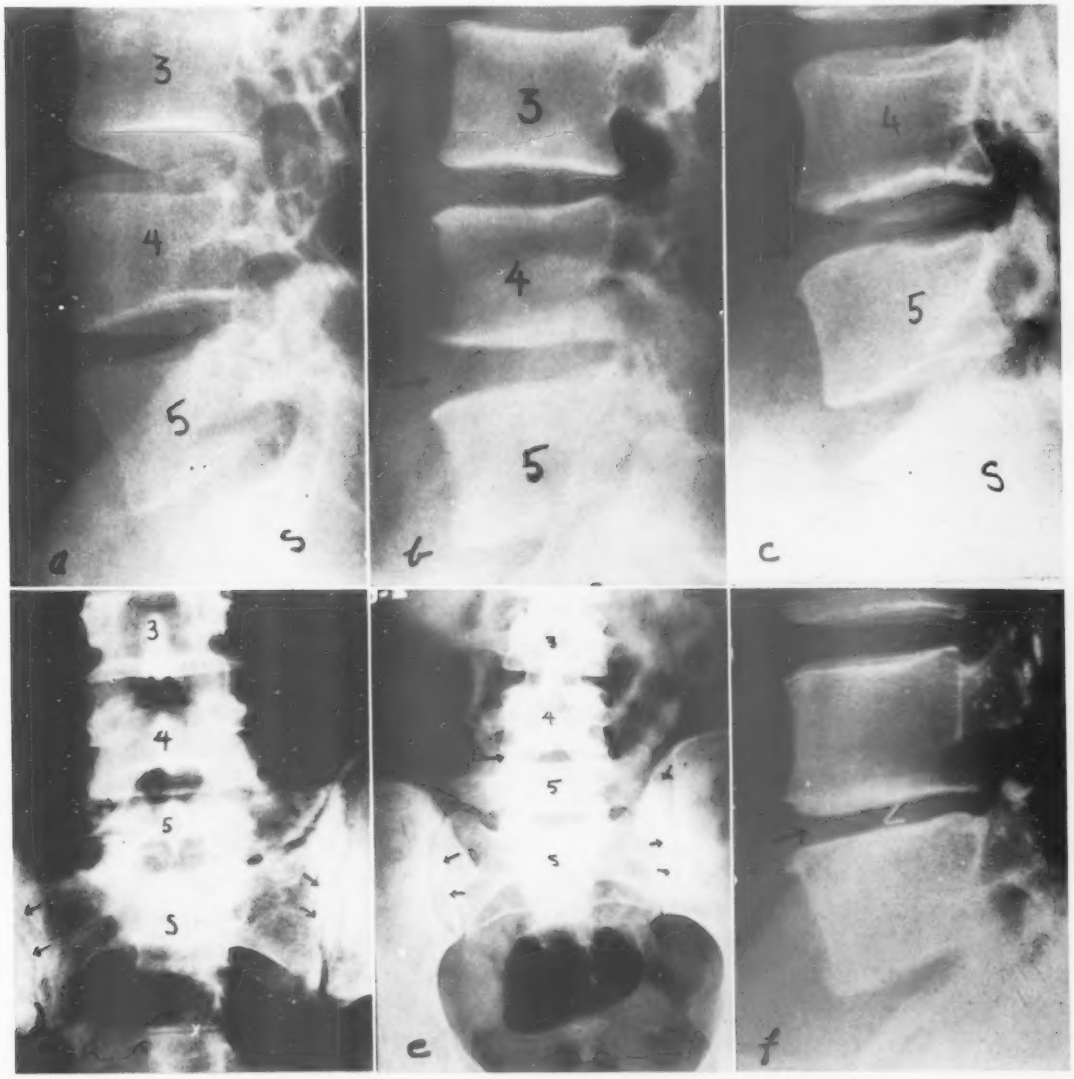

Fig. 2. A representative group of roentgenograms of patients with ruptured discs. *a*, *b*, *c*, show no significant variations from normal. The markers indicate the level and site of the lesion; *d* and *e* show that the transverse process of the fifth lumbar vertebra is sacralized and new bone formation is present about the sacroiliac joints; *f* shows a postoperative ruptured disc with a metal clip inserted into the nucleus pulposus at operation. The interspace shows the same changes that were present preoperatively.

group reported by Andrae which consisted chiefly of females over sixty years of age. He considered the large number of asymptomatic ruptures which he found in these cases at post mortem to be probably degenerative in origin. His cases also differed from ours in that 90 per cent of the ruptures in his cases occurred above L_3 disc.

Variations in alignment of the vertebrae, such as "sciatic scoliosis" and loss of the usual lordotic curve of the lumbar vertebra, are perhaps the most common variations from the normal to be noted on the routine roentgenograms. Barr first called attention to these changes and they are of value in the diagnosis when other causes can be ruled out, particularly if associated with a narrowed disc. There was definite roentgen evidence of variation from the normal in the sacroiliac joints in 2 patients (see Fig. 3*d* and *e*). The familiar Schmorl nodules in the bodies of the vertebrae were seen only occasionally.

Although Schmorl states that occasionally these posterior ruptures of the nucleus pulposus may calcify, we have noted only one such possibility which we prefer to classify as a fragment of a fractured vertebra; and for this reason this case was excluded from the series.

SUBARACHNOID INJECTION OF LIPIODOL

Former Method. Before the present method was developed 2 c.c. of fresh lipiodol was injected into the cisterna magna. A tilting roentgenoscopic table was used and no particular effort was made to demonstrate more than the usual block or "cap" formation.

By this method the first 14 patients of our series were examined. Blocks, either partial or complete, were demonstrated at the site of all the bilateral lesions, i.e., in the 4 cervical, 1 thoracic, and 6 lumbar lesions. Three unilateral lesions in the lumbar group were not demonstrated. In other words, the lesion was demonstrated in 77 per cent of the cases examined. This percentage of accuracy is greater than the 40 per cent found by Hawk, who recently reviewed the literature on this subject. We attribute our higher percentage to the use of the tilting roentgenoscopic table.

This method failed to aid in the diagnosis of the 3 unilateral lesions involving the cauda equina; therefore, after a consideration of the operative findings in these unilateral ruptures, our technique of examination was modified. This modification at first consisted of examination of the patient face down instead of face up, in order to bring the lipiodol in contact with the ventrally placed lesion and the lateral portions of the triangular canal. Roentgenograms were taken with the patient in this position both in the lateral direction, with the ray horizontal, and in the posteroanterior direction. The difficulties of demonstrating small lesions with 2 c.c. of lipiodol are obvious, and comparable to those encountered in the attempt at visualization of an extrinsic pressure defect in the esophagus by the use of a small quantity of barium. A small quantity of lipiodol is difficult to visualize because it is frequently broken up into droplets which are invisible with the roentgenoscope; a sufficient quantity cannot be manipulated to the required level, and at no time can a large enough area be covered for adequate study. Also the width of the lipiodol column does not correspond to the width of the subarachnoid space, and since the lesions in question are situated ventral to the lateral portion of the dura these areas can be studied by this method only in the oblique or lateral position, at which time false arrests are common. These modifications were found to be inadequate due to the small amount of lipiodol which we felt obliged to use because larger amounts were said to be dangerous. More and more lipiodol was injected without mishap, until 5 c.c. was used routinely.

Present Method. Five cubic centimeters of lipiodol is injected into the lumbar spinal canal. The examination may be done immediately after the injection or at any time thereafter up to several weeks. We much

prefer to do the examination on the day of injection. It may be necessary to give the patient appropriate drugs for the relief of pain so that he can cooperate in the examination. No attempt is made to maintain the patient in a fixed position after injection of the lipiodol. He is allowed to lie comfortably in bed. The equipment for the examination consists of a tilting roentgenoscopic table and a quick change-over switch so that instantaneous roentgenograms can be taken during roentgenoscopy. The usual roentgenoscopic equipment may, however, be used with fairly good results in the study of the lower lumbar area. The advantages of films taken during roentgenoscopy cannot be overestimated. Before the examination is begun the patient is allowed to sit up for a few moments in order to collect the lipiodol as one mass in the sacral cul-de-sac. He is then placed face down upon the roentgenoscopic table, and is manipulated by the use of the tilt of the table under roentgenoscopic control, the lipiodol being thus forced to flow slowly up and down the subarachnoid spaces. Particular attention is directed toward maintaining the lipiodol in a single mass, and it is possible by this method to place the lipiodol in practically any portion of the lumbar canal. If there is a questionable filling defect, an effort is made to obliterate it either by turning the patient from side to side or by repeating the tilting process. Any area which shows a constant filling defect is recorded by serial roentgenograms taken in various angles of rotation of the patient.

In every defect in this series there was complete obliteration of some portion of the lipiodol outline of the dural space. It seems doubtful if symptom-producing lesions in this area ever manifest themselves in the roentgenogram after lipiodol merely by an elevation of the ventral wall of the dural sac. Since it is often possible by the injection of 5 c.c. of lipiodol to completely fill the lumbar canal up to the inferior margin of the fourth lumbar vertebra when the patient in the upright position, this position should be used also, if possible, for the examination. If the lesion in question is included in this area there is no difficulty in demonstrating it, and roentgenograms may be taken at leisure. It is important that the examination of the lower lumbar canal be completed at the first part of the examination, because the lipiodol may break up into droplets during the course of the remaining examination. The upper and lower dorsal spine is then examined in both the prone and supine positions. Originally the upper dorsal region was usually examined in the belief that multiple ruptures of the disc might be present. This has not proved to be the case. These areas are now not examined when the patient has no symptoms referable to this portion of the spinal canal. It is possible that this may account for the infrequency of some of the untoward reactions others attribute to the use of lipiodol. The examination of these areas is, however, carried out when indicated, in the same manner as the examination of the upper lumbar and lower dorsal areas.

If a tilt table is not available, the normal lordotic curve of the lumbar vertebrae and the inclined plane of the sacrum may be utilized to force the flow of lipiodol toward the head when the patient lies face down on the table. By having the patient sit, the lipiodol may be returned repeatedly to the sacral cul-de-sac. For this type of examination it is necessary that the patient be able to shift his position rapidly, or that he be able to assume face-down position quickly without remaining for an appreciable time upon his side, because the lipiodol may already be above the site of the suspected lesion before roentgenoscopy is possible. It is also necessary that a quick change-over switch be available if satisfactory roentgenograms are to be taken. In this manner it is possible to examine the greater portion of the lumbar area, but it is practically impossible to obtain a satisfactory examination of the dorsal and cervical areas. Roentgenograms are taken at one-half second or less with 50 to 100 ma.

at 85 kv. (peak). The diaphragm shutters on the roentgenoscope are utilized for coning effect to cut out secondary radiation. It is our custom to place lead numbers on the corresponding vertebrae, and lead markers indicating "R" and "L" are fixed in position on the patient's skin so that they will be recorded on the films.

The defect may also be shown in the supine position, providing there is enough lipiodol to completely outline the defect. The lipiodol may, however, drop into the narrow posterior portion of the lumbar canal (Fig. 4), or fall away because of the convexity of the spine. This can be determined in the individual case by roentgenoscopy.

It is also possible to obtain satisfactory roentgenograms with the Potter-Bucky diaphragm and the overhead tube, providing the patient has been carefully positioned under the roentgenoscope. This is rarely necessary, however, as the "spot" films possess a wealth of detail.

Indications and Contraindications. The indications for injection have been described by Mixter and Ayer. Generally the patient has received the usual conservative measures of treatment—strapping, bed rest, corsets, etc.—but has failed to respond to these for any length of time. Although histories of remission are not infrequent in this group of cases, each succeeding attack is generally more prolonged and severe. Each of these patients is admitted to the hospital and subjected to careful orthopedic and neurologic examination. A missing ankle jerk on the affected side is considered of definite significance, as are slight sensory disturbances.

Spinal puncture and the determination of the spinal fluid protein are of considerable importance in the selection of the cases for lipiodol injection. Evidence of block is uncommon. Elevation of the total protein was present in the spinal fluid of nearly all these cases. In 32 the total was considered to be definitely elevated (over 50 mg. per cent), slightly elevated in 4 (40–50 mg. per cent) and low in 3 (below 40 mg. per cent). Although this elevation of the spinal fluid protein is usually indicative of a source of irritation within the spinal canal, it does not indicate the nature of the lesion or its level, and is subject to the limitations of any laboratory procedure. The presence of such an elevation in protein, however, justifies the injection of lipiodol in these patients. Occasionally the injection of lipiodol is carried out in spite of a low protein if the clinical findings warrant it, that is, if the patient has had some major or minor operation which has failed to relieve his symptoms, or perhaps if operation such as lumbosacral or sacroiliac fusion is contemplated.

As most of the lesions are at L_4 and L_5 the spinal puncture usually withdraws fluid from above these lesions. The total protein content decreases rapidly with the distance above the lesion. Puncture should therefore be done as low as possible.

Lipiodol injected into the spinal fluid space often produces a definite reaction, usually lasting several days, which is characterized by elevation of the spinal fluid cell count, changes in the color and chemical composition of the fluid, headache, increase in the pain of which the patient complains and slight fever. The question of the toxicity and untoward reactions resulting from the injection of lipiodol into the subarachnoid spaces has been exhaustively discussed, especially by Harkins, Globus and Strauss, Odin, Runström and Lindblom, Lindblom, and others.

Lindblom found that three weeks after the injection of lipiodol in rabbits, the cell count, which was always elevated soon after injection, had dropped to normal; further manipulations caused no subsequent rise; and sections of the cord and meninges showed no changes of note at that time, although such changes were present in the animals which were killed early.

Those who use the oil the most frequently cite the fewest reactions. Some of the reports in the literature of serious reactions to the subarachnoid injection of lipiodol are

impressive. On the other hand, Globus and Strauss, in follow-up studies of 90 cases, 25 per cent of whom were re-examined two years or more after the injection of 2 c.c. of lipiodol, reported none of the disastrous results cited by those who had used it less frequently. They state that the oil did not become encysted even after two years. Although we have used 5 c.c. (over twice as much lipiodol as is generally recommended) in 75 of our examinations we have had no serious or permanent complications; and more than 100 examinations, using 2 c.c. of lipiodol, have been done without marked reaction. The lipiodol is not always removed at operation, yet this does not seem to affect the end-results.

In spite of our own fortunate experience, we do not condone the indiscriminate injection of lipiodol into the subarachnoid spaces. Even when the criteria are quite rigid, approximately 1 in 4 patients will show nothing on examination with lipiodol. These patients are injected not because lipiodol is considered innocuous, but because the clinical and other findings suggest a lesion, and the demonstration of a lesion will lead to operative relief of their symptoms, and this probably outweighs whatever danger there may be in its use.

THE CERVICAL AND THORACIC SUBARACHNOID SPACE

Normal Anatomy. The anatomy of this region is illustrated in Figure 1a. The subarachnoid space is divided into anterior and posterior compartments by the ligamentum denticulum, and the posterior compartment is further divided by the posterior septum. It is apparent that the compartment which fills with lipiodol depends on whether the patient is prone or supine during the examination. When the patient is prone the roentgen picture is characterized by two lateral, dense bands separated by a wider band of diminished density corresponding to the region of the spinal cord. When the patient is supine the picture is similar except than the posterior septum may produce a linear central defect. Usually the separate anterior and posterior roots can be seen at their point of exit from the subarachnoid space which is marked by a corresponding pouch, or pocket, in the space. Occasionally the nerves and the radicles which form them can be seen outlined in the lipiodol shadow. This is well demonstrated in Figures 1*a* and 1*b*. These also show the lipiodol appearance of a ruptured intervertebral disc in the cervical region.

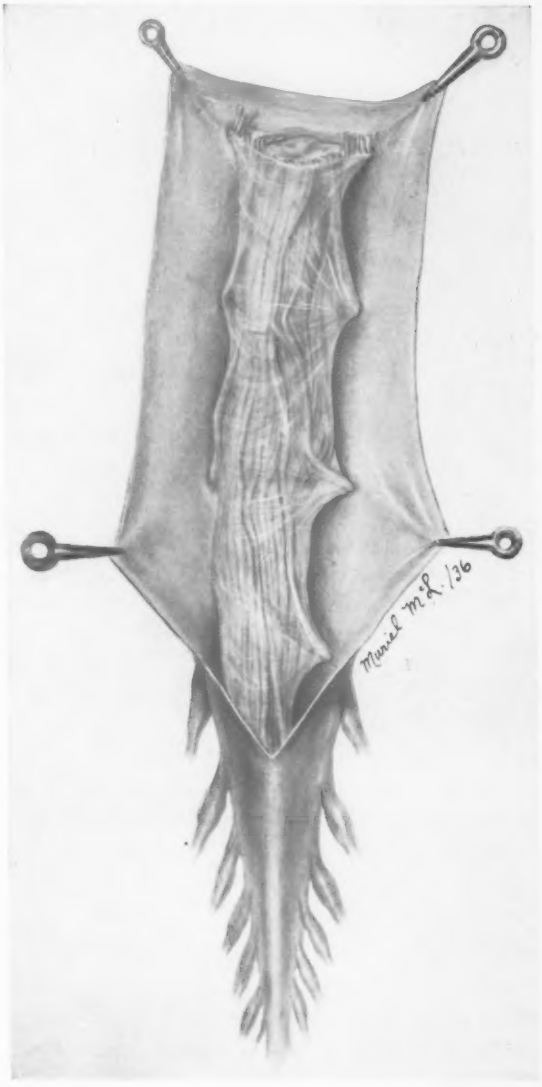

Fig. 3. The lumbar dural sac. The dura is held open by retractors. The arachnoid membrane is intact and surrounds the cauda equina, separated from it by the subarachnoid space.

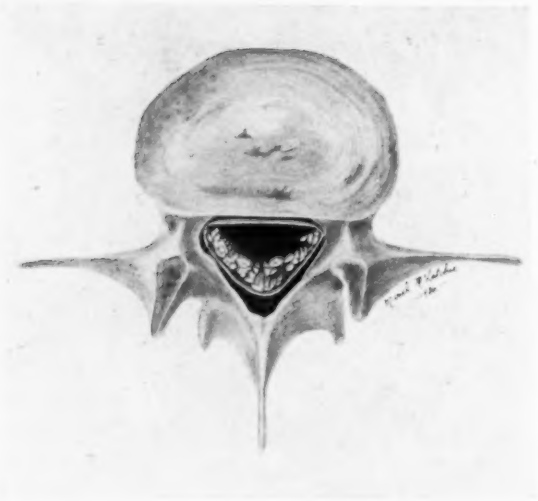

FIG. 4. Cross section through the fourth lumbar disc level. Based on a frozen section. The lumbar sac is triangular in shape. The relationship of the disc to the lamina and pedicles is shown. The nerve roots were displaced posteriorly in cutting the section.

THE LUMBAR SUBARACHNOID SPACE

Anatomical Basis of the Normal Lipiodol Picture. An understanding of the anatomical relations of the lumbar sac and the basis for the normal lipiodol picture in this area is desirable, as this permits one to more accurately interpret the defects produced by lesions and to recognize and establish the identity of the individual nerve roots involved.

Anatomy. Figure 3 shows the lumbar sac with the dura opened; the transparent arachnoid membrane is intact, and the dura is held open by retractors. There is only a potential space between the dura and arachnoid, the two membranes forming the wall of the "dural" sac. The space between the arachnoid membrane and the nerve roots is the subarachnoid space into which lipiodol is injected. Where each root leaves the dural sac there is a distinct drawing out of the arachnoid membrane. The apex of this out-pocketing is marked by the close attachment of the meninges, which continue along the nerve roots as the sheath.

The nerve root usually fills the upper part of its corresponding arachnoid pouch. Usually it is in contact with the lateral wall of the pouch and sac for a short distance. The roots have been disarranged in preparing the specimen from which this drawing was made. Normally they are symmetrical.

Figure 4 is a drawing based on a frozen section through the fourth lumbar disc level. The cauda equina was apparently displaced backward in cutting the section. The triangular shape of the canal and the

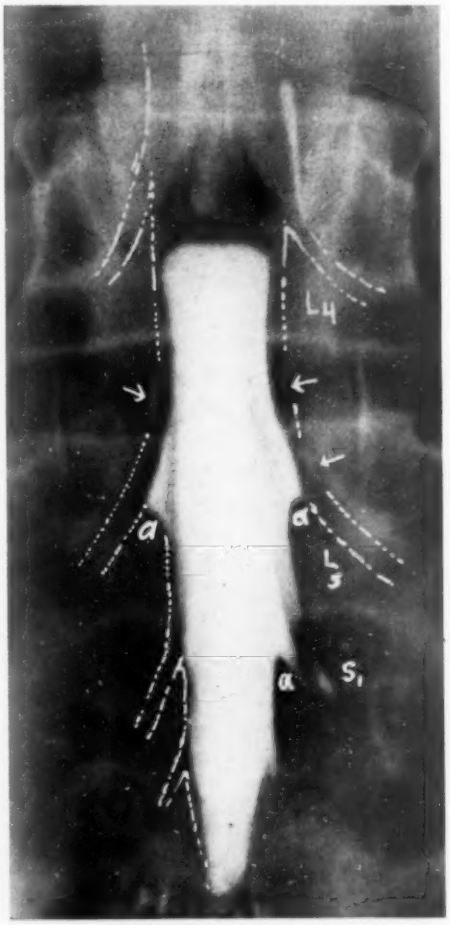

FIG. 5. Normal filling of the lower lumbar subarachnoid space. Five cubic centimeters of lipiodol produces filling of the lumbar canal from the fourth lumbar vertebra to the second sacral segment with the patient standing. The course of the nerve roots has been drawn in to correspond to the anatomic findings. Note normal filling of S1 nerve root sheath and the axillary pouches.

sac and the relation of the latter to the disc and the bony canal should be noted.

Normal Roentgen Picture after Lipiodol. Although there is little variation in the anatomic appearance of the subarachnoid space, there is a marked variation in the corresponding roentgen picture. This is caused almost entirely by the amount of lipiodol employed and by the close contact of the nerve root to the lateral wall of the sac. This contact prevents filling of this portion to a greater or lesser degree so that some part of the root rather than the wall of the lumbar sac frequently forms the lateral outline of the lipiodol picture. Complete filling is rarely seen except above an obstruction produced by a lesion, although examination carried out several days after the injection of lipiodol usually shows fairly complete filling of the lateral portions of the subarachnoid space.

Fig. 6. The course of the nerve roots. Wires have been attached to the individual roots of the cauda equina on one side and pins inserted through the sheath portions of the roots on the other. Each root follows the under border of the pedicle into its respective foramen.

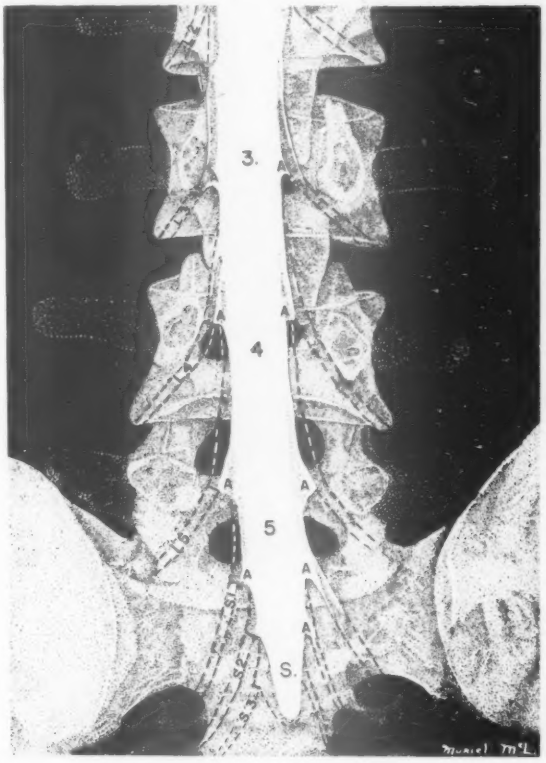

Fig. 7. Key chart. A composite of numerous roentgen examinations after the injection of lipiodol showing the variations which occur. The course of the nerve roots has been drawn in and each root labelled. This illustrates the method by which the roots are identified.

Figure 5 is a representative roentgenogram after 5 c.c. of lipiodol, the patient standing. Numerous pouch-like projections are seen laterally. On the right S1 root is well outlined by lipiodol in the sheath.

The projections in the lipiodol picture correspond only to that portion of the subarachnoid out-pocketings which fill with lipiodol. The lower portion which contains no anatomical structures usually fills readily, forming the triangular areas seen on the

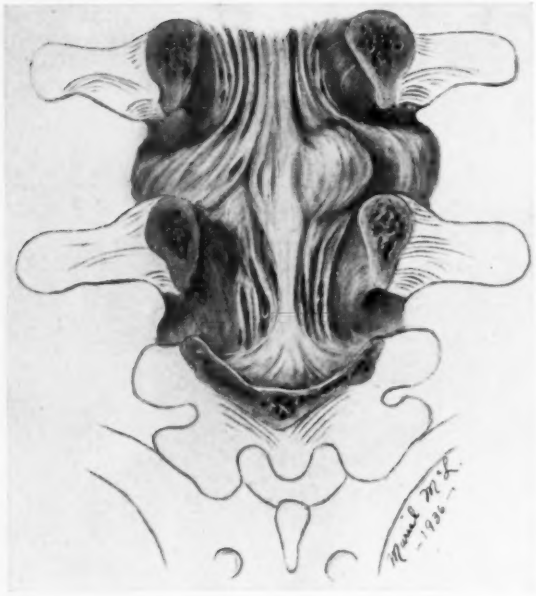

FIG. 8. Unilateral posterior rupture of fourth lumbar disc. The dural sac and its contents have been removed, exposing the posterior longitudinal ligament (somewhat exaggerated) and ventral surface of the vertebral canal.

film. The upper portion fills to a varying degree. The apices of these projections are useful anatomical landmarks for they mark the beginning of the lower border of the nerve sheath. We have therefore termed them the "axillary apices," and on the roentgenograms they are indicated by the letter "*a*." Not infrequently the lipiodol which fills in the space between the nerve root and the lateral wall of the sac gives the impression that the root lies apart from the sac, but actually it is within it; the nerve sheath originates at the apex of the pouch. By drawing a line from the axillary apex across the nerve outline the sheathed portion of the nerve can be separated from the part within the lumbar sac. If the nerve outline is not visible it can be determined readily by utilizing the constant relationship which the lateral wall of the sac and the sheathed portion of the nerve bears to the inner border of the pedicle. This relationship is illustrated in Figure 6. Wires have been tied to the roots of the cauda equina on one side and pins inserted through the sheathed portion of the roots on the opposite side. Each root follows the inner border of the pedicle into the corresponding intervertebral foramen. This relation is quite constant and symmetrical, and can be utilized to identify the lateral border of the sac and the nerve roots since the root is named by the intervertebral foramen through which it passes.

This is well illustrated in Figure 5 in which these *pedicle lines* have been drawn in. If these are correctly drawn they should correspond to the streaks of lipiodol which are seen outside the main column. In this manner it is possible to determine the nerve roots involved by a lesion in this area. Thus, at L4 disc the lateral root is L5; the root medial to it is S1, etc. At L5 disc the lateral root is S1 and the root medial to it is S2, and so on.

The Anatomical Basis of the Lipiodol Defect (Figs. 8, 9, 10 and 11). Figure 8 illustrates a posterior rupture of the disc at L4 interspace. The contents of the lumbar

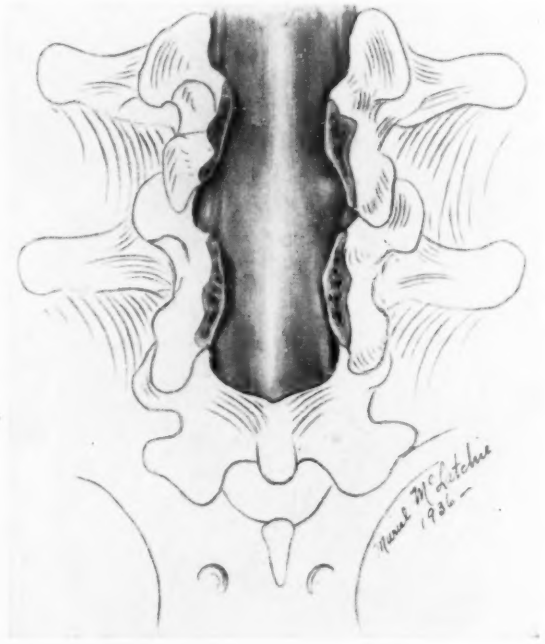

FIG. 9. Appearance of the ruptured disc after laminectomy before removal of base of lamina and articulating facets. The dural sac is elevated by the nodule beneath it. The lateral portion of the sac and the root (L5) is wedged against the base of the lamina and articulating facet.

canal have been removed and the posterior longitudinal ligament on the anterior wall of the vertebral canal is visible (rather exaggerated). Unilateral ruptures usually take place at one side of it. The relation of the rupture to the narrow lateral portion of the vertebral arch should be noted. Generally such a lesion is rounded or nodular in shape and about 1 cm. in diameter. It may vary considerably in size and project in any direction. It is the strategic position of the lesion with reference to nerve roots rather than its shape or size which is important.

Figure 9 illustrates the typical appearance of the lesion at operation before the removal of the bases of the laminae and the articulating facets. The lateral portion of the sac is elevated and compressed against the roof and edge of the base of the vertebral arch. The compressed nerve root is barely visible wedged against the sharp edge of the base of the facet.

Figure 10 shows the appearance of the lesion after the removal of the base of the arch, including the adjacent portion of the facet. The bulge in the dura is exaggerated somewhat as usually the lesion is not perceptible until the dural sac has been opened or retracted. The normal and the compressed roots are well seen. It should be noted that the nerve root does not leave the lumbar sac until it is below the disc, although its outline can be distinctly seen in the lateral portion of the sac. As the nerve root leaves the sac somewhat ventrally, the bulging edge of the dural sac further accentuates this pseudo separation of the root from the main sac, so that at operation the sheath may appear to originate higher than is actully the case.

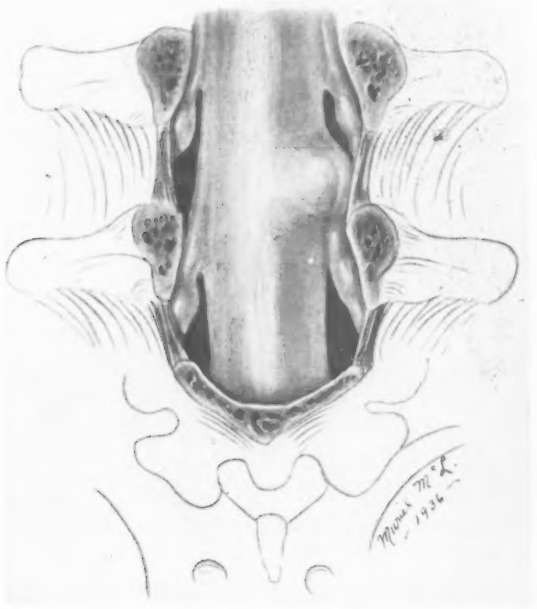

Fig. 10. Appearance after removal of pedicle and a portion of the facets. These drawings show bilateral laminectomy, although unilateral laminectomy is usually done.

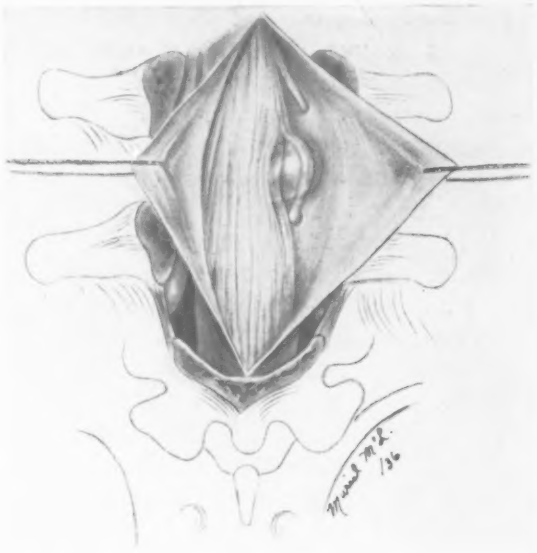

Fig. 11. Appearance after opening the dura. The relation of the intradural roots to the extradural mass is seen. Compare this figure with the roentgenograms taken after the injection of lipiodol.

Figure 11 illustrates the appearance of the same lesion with the dura open. By comparing it with the two previous figures it will be obvious that the compressed nerve root (L_5) is intradural in its entire course across the L_4 disc. This relation is of considerable importance. It indicates that it is very unlikely for a ruptured disc at L_4 to compress L_5 nerve root without at the same time compressing the lipiodol containing lumbar sac. Involvement of L_5 root by a ruptured disc is therefore relatively readily demonstrable. A rupture of

L5 disc will not compress L5 root because the latter leaves the vertebral canal above this disc, but will compress the first sacral root which does cross this (L5) disc. As this root (S1) acquires its sheath between the upper and lower border of L5 disc it is not entirely within the lipiodol containing lumbar sac in its course across it. Therefore a lesion at L5 may compress S1 root without producing a defect comparable to the size of the lesion. The relations of the sacral roots are well shown in Figures 5, 7 and 26.

The Characteristic Lipiodol Defect. The four figures just described (Figs. 8, 9, 10 and 11) indicate the various features which play a part in producing the "characteristic" defect, a defect produced by a mass ventral to the dural sac, to one side of the midline, which elevates the lateral portion of the dural sac and compresses it and its contents against the roof and sides of the narrow lateral portion of the vertebral canal. The nodule in Figure 11 is immediately cephalad to the point at which the nerve is fixed to its sheath. Compression at this point therefore involves this nerve root. The latter rides directly over or to one side of the nodule. Although in this case the root is displaced laterally (Figs. 10 and 11) the lesion is definitely anterior to the dural sac. If the nerve root rides on the medial side of the nodule it is pushed under the sac "from behind" although here again the lesion is anterior to the dural sac for the most part.

By studying Figure 11 one can readily determine the mechanism which produces the lipiodol defect. As can be seen in the following roentgenograms small concavities are frequently seen on the upper border of the lipiodol defect which corresponds almost perfectly to the appearance of the roots at the upper border of the lesion shown in Figure 11. Almost invariably in such cases the edges of two nerve roots can be distinguished. Sometimes the combined outline of the compressed edge of the two roots may appear as one widened root and careful examination may be necessary to distinguish them. Although edema of the roots is described at operation such a diagnosis is probably not justified in the interpretation of the lipiodol picture unless the definitely widened outline of the root can be seen for a considerable distance above the defect, standing out in the same way as a thickened rugal marking stands out in the barium-filled stomach.

Usually the medial border of the defect is formed by the outline of a nerve root. Deviations of the compressed roots in a medial or lateral direction are difficult to determine as they occur in the area from which the lipiodol has been expelled. The lipiodol picture, as has been stated, shows the edge of two roots on the upper margin of the defect and the clinical picture seems to favor the involvement of two roots. At operation, however, compression of only the laterally placed root is often found. Probably this is accounted for by the fact that the laminectomy decompresses the more medially placed of the two roots. That the compression of the second root as seen on the lipiodol picture is not a temporary phenomenon due to incomplete filling is shown by the fact that a patient may be examined in the upright position, or examined several days apart, without obliterating the defect.

Contrary to expectation, the lateral view often gives surprisingly little information. If the lesion is unilateral it does not elevate much of the sac across the midline. In the lateral view, therefore, only a slight defect may be visible; the defect on the involved side is obscured by the dense lipiodol in the remainder of the sac. In difficult cases, however, the demonstration that a defect seen in the anteroposterior view is produced by ventral, extradural (i.e., "extrinsic") pressure is particularly important as defects similar to those produced by ruptured disc are occasionally produced by arachnoiditis. In the lateral view, however, these usually show a sharp edge due to their intradural nature. The defect seen in the lateral view should probably never be interpreted as indicating a pathological con-

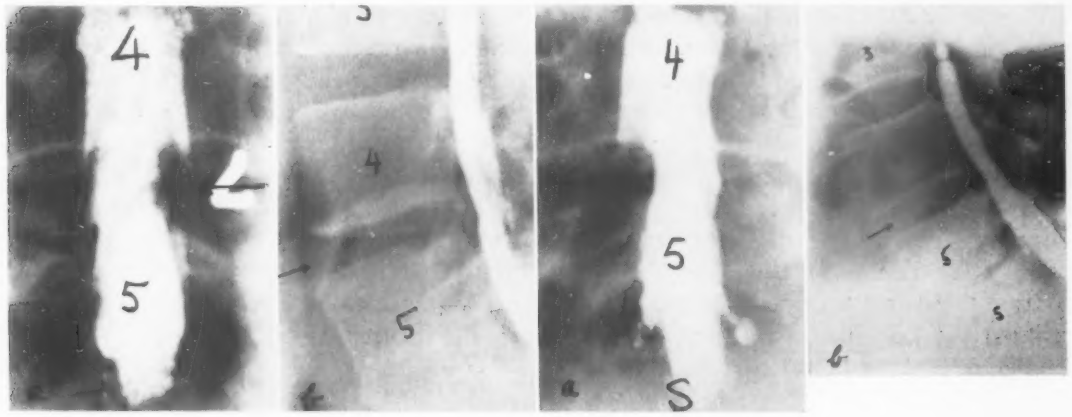

Fig. 12 Fig. 13

Fig. 12. *a*. Defect produced by ruptured disc. Two nerve roots (L5 and S1) can be distinguished on the upper border of the defect; *b*, lateral view. Only a slight defect is seen. It is ventral and extradural. Joint space is narrowed.

Fig. 13. *a*. The upper margin of the defect is smooth, although an area of diminished density is seen suggesting compressed roots. The defect extends higher than that in Figure 12; *b*, defect is barely seen due to superimposed lipiodol. Note the narrowed L5 disc.

dition unless associated with an anteroposterior defect since normal bulges of the intervertebral disc may produce similar variations in this view.

Characteristic lesions will now be described by the use of illustrative roentgenograms, separating L4 and L5 defects because of certain differences in their appearance caused by the anatomical differences we have mentioned.

L4 Defects. In Figure 12*a* the outline of a normal nerve can be made out on the right side, the lipiodol extending almost as far as the origin of the sheath. On the opposite side a defect is seen obliterating the axillary pouch. A close study of the upper

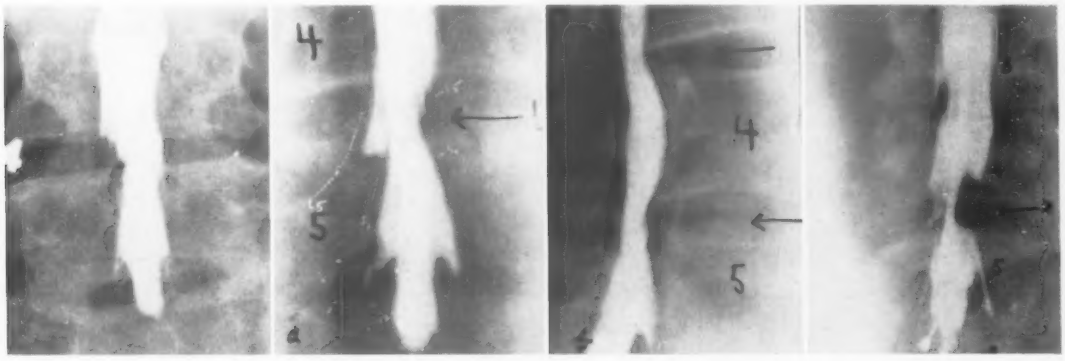

Fig. 14 Fig. 15 Fig. 16

Fig. 14. Two normal roots (L5 and S1) are seen at the upper margin of the defect. S2 root is seen on end medially.

Fig. 15. *a*. This defect is similar to that in Figure 14 except for a normal difference in the lipiodol appearance of the lumbar sac; *b*, the pseudo defect at L3 was not present in the lateral view and is of no significance.

Fig. 16. The broad band of diminished density above the defect apparently represents two swollen nerve roots (L5 and S1) and the smaller one below a swollen S1.

border will show that it is formed by L5 root laterally and S1 medially. The latter is continuous with the outline of S1 below the defect. The lesion does not extend to the upper margin of the disc. The lateral view shows a slight extradural defect in the ventral surface of the lipiodol column. In Figure 13*a* the defect extends to the upper border of the disc.

Figure 14 shows a defect similar to that in Figure 13, except that definite small or posterior defect in the oblique view. In this case as in others this false defect was not present in the lateral view.

If the nerve roots are swollen the appearance may be exactly as it is in Figure 14 except that the shadows of the roots are wider. In Figure 16 a broad linear band of diminished density extends upward for a considerable distance above the defect. Below, S1 is seen outlined, and it is obviously widened, but its width is less than that of

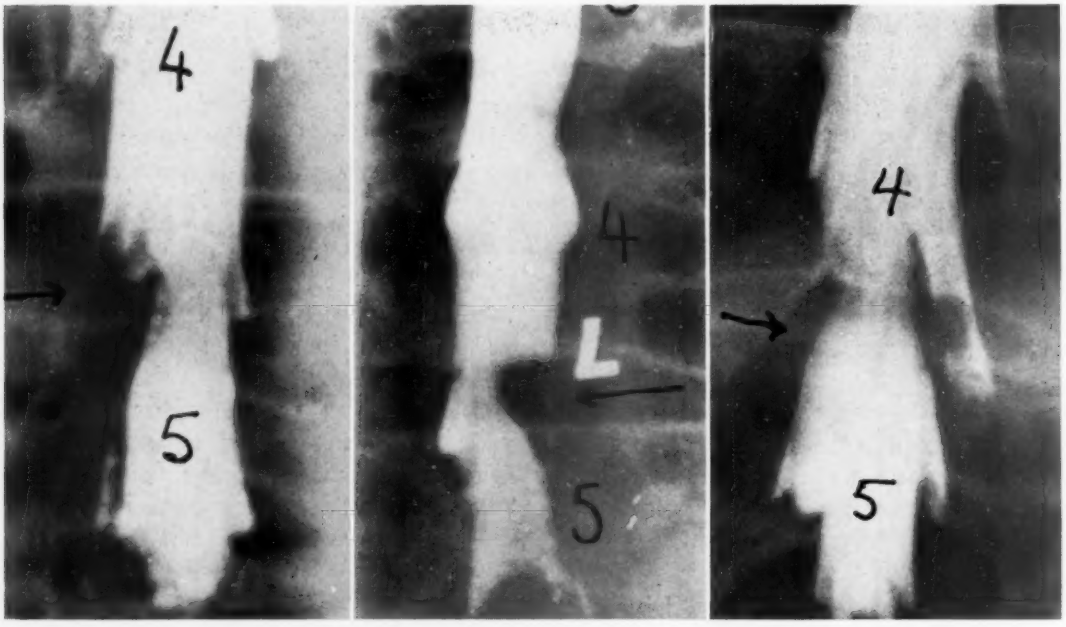

FIG. 17 FIG. 18 FIG. 19

FIGS. 17 and 18. There are two nerve roots (L5 and S1) at the upper margin of the defect. Compare this defect with the lesion shown in Figure 11.

FIG. 19. A unilateral rupture extending across the midline.

concave pressure defects corresponding to two nerve roots, L5 and S1, are seen. The lower medial indentation is produced by S2 seen on end.

Figure 15 shows a defect differing only from the previous case in the variation produced by a normal difference in the lipiodol appearance of the sac. In the oblique view defects are seen at L3 and L4 (Fig. 15*b*). Such false defects are frequently seen in this view. A normal "waisting" in the anteroposterior view may appear as a ventral the band-like shadow above. By careful study the outline of L5 and S1 could be separated above the defect. The curve of the sac in this case, as in many others in the series, is exaggerated by scoliosis.

Although a larger defect may be produced, rarely are the roots of any but the lateral two nerves seen. This is shown in Figure 17. The two serrations at the upper border of the defect and the defect itself corresponds almost exactly to that expected in the lesion shown in Figure 11. The

serrations correspond to L5 and S1 roots.

Many of the cases do not show the serrations produced by compressed or swollen nerves, but instead there is a sharp upper margin. Thus Figure 18 is similar to Figure 17, except for the absence of the serrations. There is a common picture. The absence of the nerve root defects is due to the degree of filling. Sometimes this appearance is seen early in the examination, whereas films taken later show the separate outlines of the roots. It is obvious, regardless of whether or not the roots can be distinguished, that these defects with their sharp upper border are not produced by any significant degree of lateral pressure on the dural sac.

Sometimes these lesions, though unilateral and associated with unilateral symptoms, may extend almost across the midline, as can be seen in Figure 19; or they may extend so far over as to produce practically a block as in Figure 20. The type and severity of the patient's symptoms depend upon the nature of the nerve root compression rather than the size of the lesion.

Occasionally a lesion may seem to be opposite the center of a body instead of the disc, although it will be noticed that all the lesions so far described are obviously at the disc level. When the lesions appear to be opposite some portion of the body of the vertebrae, as in Figure 20, careful study will usually show that this is due to lordosis of the lumbar spine, although it is possible for a ruptured nodule to find its way above the disc beneath the longitudinal ligament as described by Schmorl.

Figure 21 shows a similar defect crossing the midline. Part of it is formed by a ruptured disc and part by a generalized protrusion of the disc on this side into the canal. There is complete filling of the sac above a partial block. The lateral edges of a filled sac occupy the spinal canal and extend to the border of each pedicle. This degree of

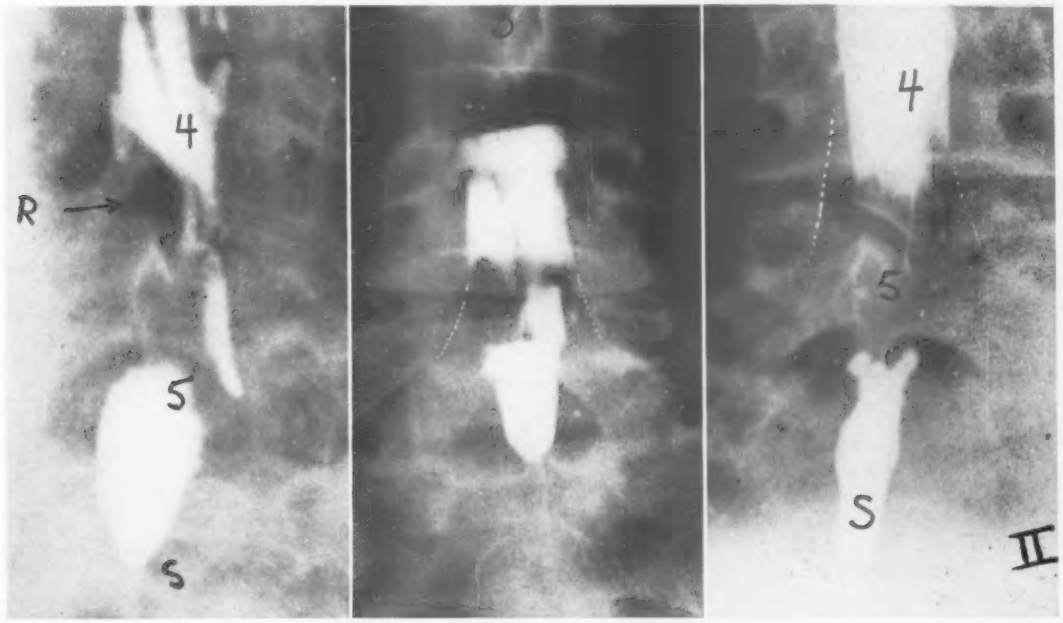

Fig. 20 Fig. 21 Fig. 22

Figs. 20 and 21. The lesions, although extending across the midline to practically produce a block, were associated with unilateral symptoms. Note the complete filling of the sac above the lesion in Figure 21.

Fig. 22. A bilateral lesion. The edge is ragged and is apparently formed by compressed roots. The defect extends below the disc level.

filling is in contrast to that usually seen associated with smaller defects, where complete filling is present only above and on the same side as the lesion.

The defect illustrated in Figure 22 is characteristic of many of those associated with bilateral symptoms of tumor of the cauda equina. The ragged edge strongly suggests compressed nerve fibrils. This edge is unlike the "cap" produced by an intradural tumor.

is intradural as it crosses the disc. When the defect at L5 is small it usually shows a characteristic appearance as though the root had been pinched off at its origin. As the second sacral root runs for some distance in the vertebral canal before making its exit, it is more or less readily displaced in a medial direction by the ruptured disc and this may be visible in the roentgenogram taken after the injection of lipiodol. Because the lipiodol does not find its way

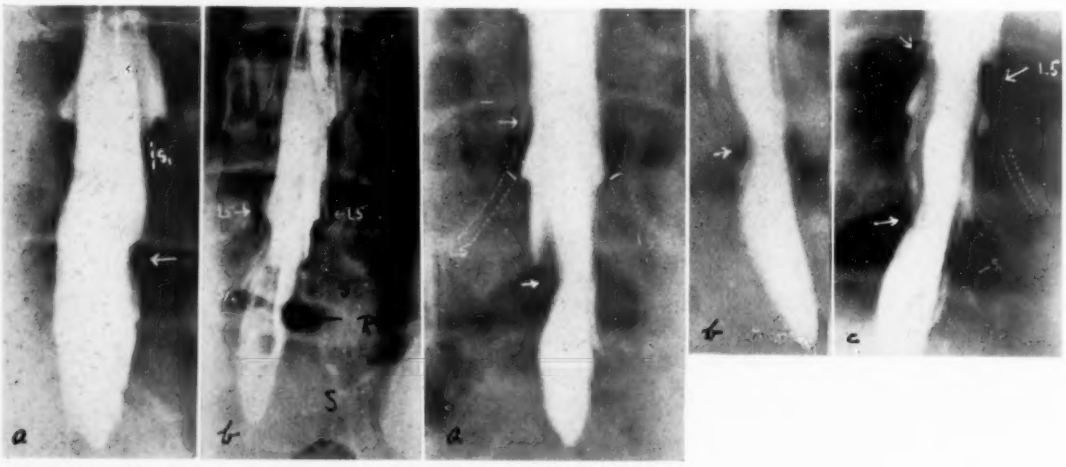

FIG. 23 FIG. 24

FIG. 23. *a*. A small defect at L5 produced by a large ruptured disc; *b*, the same patient six months later (also preoperative). More complete filling of nerve roots. Defect still present.

FIG. 24. *a*. Defect produced by rupture of L5 disc; *b*, defect well demonstrated in the oblique view; *c*, same defect one week later (also preoperative). Defect has changed its appearance because of more complete filling but is constant. Note the upper border of the defect was formed by S1 and S2 (which is displaced medially).

L5 Defects. The L5 defects are usually more difficult to demonstrate and interpret than those previously described. Not only do L5 defects differ because of the anatomical relationships—i.e., the origin of the sheath of the root above the lower margin of the disc and the size of the sac in this region—but not infrequently they are quite broad and flat, rather than round and circumscribed. As we have stated, it is possible for a lesion at this level to lie under the nerve root beyond its point of origin from the main sac without producing a corresponding defect in the sac, whereas this is not likely at L4 because the nerve root easily between the compressed walls of the sac the defect is usually quite sharp in outline, but if the patient is examined at a later date, filling in between the walls of the sac is not infrequently seen.

A very small defect is shown in Figure 23*a*. This defect alone was not sufficient indication for operation, particularly as the spinal fluid protein was only slightly elevated. Instead, fasciotomy was performed. Six months later the patient was re-examined due to continued symptoms. Figure 23 shows the defect previously noted. It was also noted that whereas the nerve sheaths were filled on the normal

side they remained unfilled on the involved side. As the interval between the examinations was long, and the sheaths at this level normally tend to fill rather readily even at a first examination, this was considered significant, although more significance was, of course, attached to the constancy of the defect. At subsequent operation a good sized rupture was found at the point indicated, the lesion lying directly anteriorly. Other lesions of this type have been seen in which re-examination was helpful; but it must be emphasized that we have not diagnosed a rupture of the intervertebral disc solely on the findings at re-examination. If the defect represents a lesion it is constant and should be demonstrable at any time. The filling of the nerve sheaths and the other phenomena sometimes seen on re-examination are occasionally of accessory value. Figure 23*a* and *b* also illustrates more complete filling of the lateral margin of the sac which occurs with time. If the pedicle lines are traced in they will indicate the changes.

Figure 24*a*, *b* and *c* shows changes similar to those in Figure 23 which may take place between examinations. In both these cases the lesion was directly anterior to the lumbar sac. The changes noted in Figure 24 occurred in one week. In the oblique view (Fig. 24*b*) the lesion is well demonstrated. The lipiodol originally injected sufficed for the second examination in both cases.

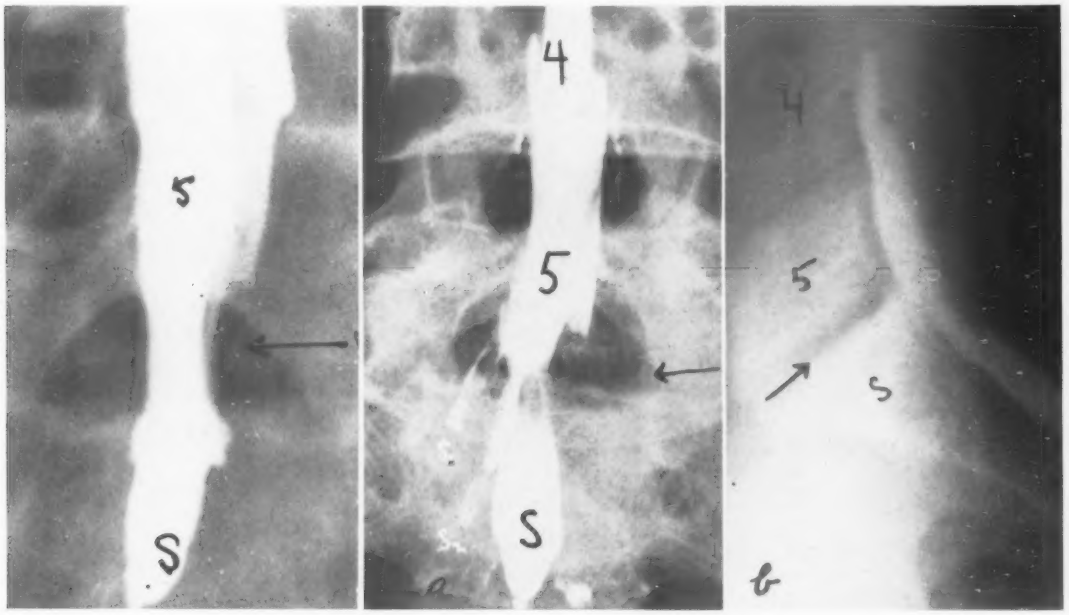

Fig. 25 Fig. 26

Fig. 25. Root defects (probably swollen S1 and S2) are well shown above the main defect.

Fig. 26. *a*. Normal complete filling of S1 and S2 nerve sheaths on normal side and large defect opposite. Note relations of the sheaths to the disc; *b*, the defect demonstrated in the anteroposterior view is not seen in the lateral view.

Figure 25 shows a similar defect except that the roots seem swollen.

Figure 26*a* shows a defect at this level similar to those seen at L4. The lesion is not seen in the lateral view (Fig. 26*b*). In this, as well as in Figure 23*b*, the filling of the nerve sheaths is absent on the side of the lesion. (Compare the filled sheaths in Fig. 26*a* with those of Fig. 5.) The pedicle lines indicate that S1 and S2 nerves were involved and this corresponded to the operative findings. In this case a round

mass of disc fibrocartilage, 1.5 cm. in diameter, was found lying free anterior to the dura. The size and shape of the lipiodol defect corresponded to these findings. Generally the nodule of the ruptured disc is found attached to the remainder of the disc and in these cases it is necessary to compare the roentgen findings after the use of lipiodol with the size of the intact nodule before its removal. Predictions made concerning the size of the lesion from the lipiodol picture are unsafe, as a good portion of the rupture may be beyond the lipiodol containing dural sac. A large defect usually means a large lesion; a small defect may be produced by a small or large lesion.

particularly if associated with narrowing of the interspace, and four errors were made as a result of this supposition.

In Figure 29, the defect shown should not be regarded as due to ventral pressure and therein differs from the pressure defect of a ruptured disc. At operation, a fracture of the adjacent laterally placed pedicle was found.

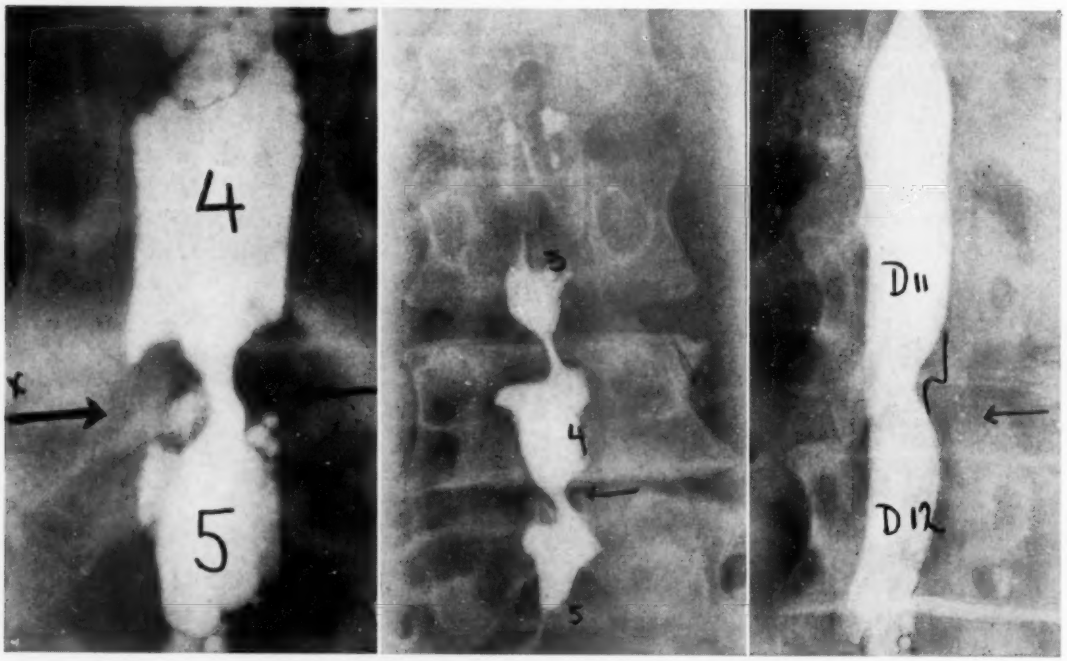

FIG. 27 FIG. 28 FIG. 29

FIG. 27. The defect is actually produced by protrusion of the entire disc although the appearance is that of ruptures to both sides of the midline.

FIG. 28. An atypical picture produced by arachnoiditis complicating a ruptured disc.

FIG. 29. The defect is due to lateral pressure from a fractured pedicle.

DIFFERENTIAL DIAGNOSIS

At one time it was felt that definite constant defects at intervertebral levels indicated rupture of the intervertebral discs,

Multiple constrictions of the lipiodol column opposite the disc levels were seen in 2 cases. These were explained by arachnoiditis, which was found at operation. One of these cases is illustrated in Figure 27. In addition to arachnoiditis, a rupture of L_4 was also present at the site of the defect indicated by the arrow. This defect is similar to Figure 23*a*. However, intra-arachnoid changes could probably produce such an appearance.

We have noted one lesion which we at-

tributed to a fragment of a fractured vertebral body that produced a picture indistinguishable from a ruptured disc.

Tumor has not infrequently been diagnosed in patients with complete block, because with the patient in the Trendelenburg position the lower border of the lesion is well below the level of the disc. This appearance is produced by compression of the nerve roots below the disc against the bony arch similar to that described for the unilateral lesions.

Complete hypertrophy of the posterior margin of the disc is shown in Figure 27. Because the amount of protrusion is uniform across the width of the disc, the lateral portions of the canal are obliterated, and the central portion remains as a narrow canal. This appearance is due to the triangular shape of the lumbar sac (Fig. 4). Although this picture is consistent with a true bilateral rupture of an intervertebral disc, at operation only marked hypertrophy of the posterior margin of the disc was found. In both this case and a more recent similar one, definite narrowing of the interspace was associated with the lesion. This uniform bulging of the disc posteriorly possibly explains the small, symmetrical defects which are frequently seen. The exact significance of these small defects, however, has not yet been determined. Thickening of the ligamentum flavum was found associated with a ruptured disc in 3 cases. Two of these showed complete block. In one case a ringlike extradural defect was demonstrated. This is shown in Figure 30 *a* and *b*. The characteristic defect has been modified by the presence of the thickened posterolateral ligamentum flavum. The entire defect is definitely extradural.

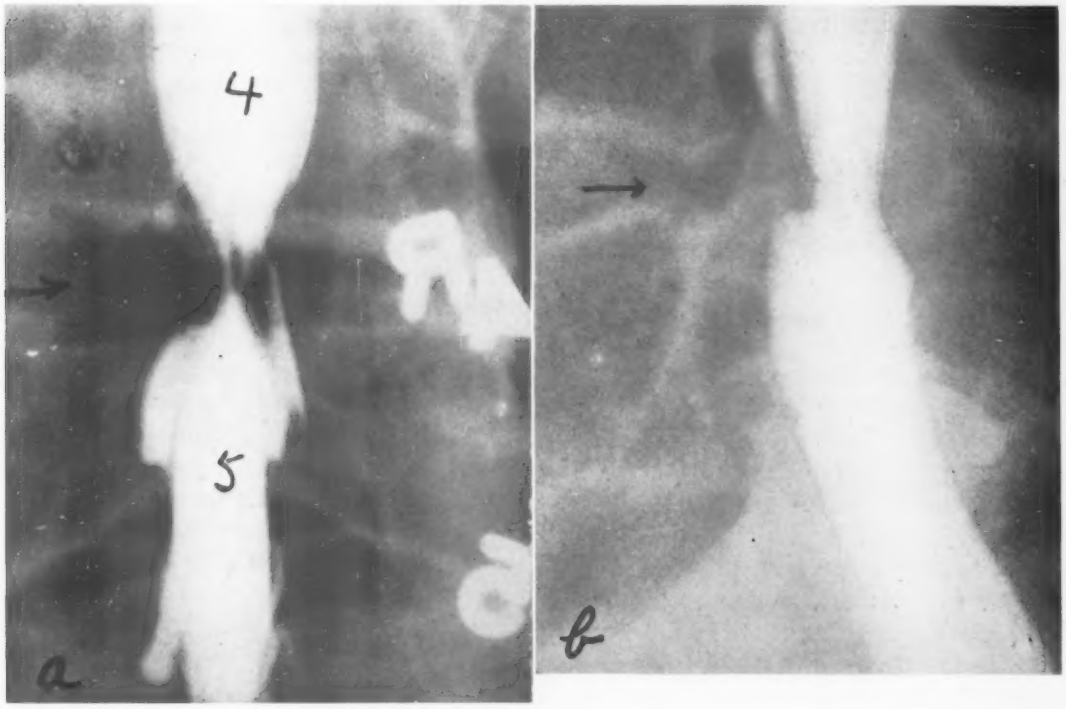

Fig. 30. *a*. Unilateral rupture of the disc complicated by thickening of the ligamentum flavum, which has modified the defect; *b*, ring-like defect in lateral view formed by ruptured disc anteriorly and thickened ligamentum flavum posterolaterally. Note narrowed disc.

Accuracy of Present Method of Examination and Diagnosis

By the use of the present method of

examination, definite variations from the normal have been demonstrated in all the 31 consecutive cases of ruptured disc operated upon in the past three years, but as one of these was not recognized preoperatively it has been classified as "not demonstrated." An outright diagnosis of rupture of the intervertebral disc was made from roentgen findings after the use of lipiodol in 23. Of the unilateral lesions, 22 were demonstrated as unilateral defects, 20 of which were sufficiently characteristic to justify the roentgen diagnosis of ruptured disc, because unilateral ventral extradural lesions at the disc level other than these ruptures are quite rare. When the appearance was complicated by arachnoiditis or when the lesion extended across the midline it has generally been reported as tumor as the defects seemed to be too large to be produced by disc. The explanation for this finding has already been given. There were 4 surgical explorations for ruptured disc in which both the surgical and roentgen findings were negative. Other errors in differential diagnosis have been mentioned above, and as stated in the beginning of the paper the 3 unilateral lumbar lesions examined in previous years by the old technique were not demonstrated. In only 1 case was an adequate explanation for the roentgen picture not found at operation.

SUMMARY

The roentgenological findings in fifty patients operated upon at the Massachusetts General Hospital for the relief of symptoms of spinal cord or nerve root compression caused by the protrusion of a portion of an intervertebral disc into the spinal canal have been described.

The value of lipiodol examination has been stressed, for by such examination it was possible to demonstrate the presence of a lesion in 30 of 31 patients operated upon in the past three years, although practically all of these cases were unilateral ruptures of the lumbar discs producing no significant block. This demonstration was of the utmost importance in the differential diagnosis because the clinical picture was that of low back strain, sacroiliac strain, "sciatica" or some similar condition.

The findings on the usual roentgenograms, the technique of lipiodol examination, the correlation of the surgical and roentgen findings, a study of the anatomical relations of the nerve roots and an explanation for variations in the normal picture after lipiodol in this area are presented and a method of interpretation described based on the recognition and identification of the individual nerve roots.

CONCLUSIONS

From the material presented in this paper the conclusion seems justified that examination of the subarachnoid space after the injection of lipiodol is of *definite* importance in the differential diagnosis of all symptom-producing ruptures of the intervertebral discs into the spinal canal, and is of *paramount* importance in the differential diagnosis of unilateral lumbar ruptures accompanied by low back pain with "sciatic" radiation.

A correlation of the clinical, laboratory and roentgen findings after the injection of lipiodol should permit an accurate preoperative diagnosis of posterior rupture of the intervertebral disc in nearly every case.

The drawings and photographs are by Miss Muriel McLatchie, medical artist, and Mr. Wilbour Lown, photographer, Massachusetts General Hospital.

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UNUSUAL FINDINGS IN A CASE OF CHARCOT'S ARTHROPATHY

By A. BRADLEY SOULE, JR., M.D.
BURLINGTON, VERMONT

IN 1868 Charcot[1] published his original description of the disease characterized by a peculiar painless disorganization of joints, occurring in the course of some cases of tabes dorsalis. This condition has been variously named "Charcot's tabetic arthropathy," "neuropathic arthritis," "arthropathy of peripheral nerve lesions," etc. While the disease was formerly thought to occur solely in association with tabes,[2] it is now known that it may occur in syringomyelia and in other conditions in which there is a loss of trophic nerve supply to a joint. Shands[6] has reported a case of arthropathy of the ankle due to a peripheral nerve lesion. Israel[3] has described changes similar to Charcot's arthropathy in patients with tumors of the spinal cord, and following severance of the cord.

FIG. 1. Right hip. Note rib-like spur of bone extending upward toward the right kidney area.

In tabes, the lesions are usually single. Wile and Butler,[7] in reporting a series of 88 cases, found monarticular involvement in 72 per cent. Of the remaining 28 per cent which showed multiple lesions, bilateral involvement was found in more than two-thirds. Polyarticular involvement occurred commonly in cases where small joints (i.e., wrist, hand, ankle and foot) were affected. In this same series, the joints most commonly affected were the knee (66 per cent) and ankle (25 per cent). The spine was involved in about 7 per cent, the hip in 6 per cent and the shoulder in 5 per cent, with the small joints showing changes in less than 6 per cent of cases. Most other investigators have reported involvement of the joints of the lower extremity in 75 to 80 per cent of cases. This is due to the fact

FIG. 2. Left shoulder. An old spiral fracture of the shaft of the humerus is present in addition to the characteristic arthropathic changes in the shoulder.

that the tabetic cord lesions are usually in the lumbar segments of the spinal cord.

In syringomyelia, the shoulder, elbow, wrist and hand joints are more commonly affected due to the usual high location of the lesion (lower cervical and upper dorsal).

The disease is more commonly seen in males, and usually appears between the thirtieth and fiftieth year. It frequently occurs early in the course of tabes.

The mechanism of production of the disease is obscure. It seems to be definitely associated with loss of trophic nerve supply to the affected joint or joints. Most investigators support the theory that the loss of pain sensations in the joint allows trauma to occur which otherwise would be avoided.

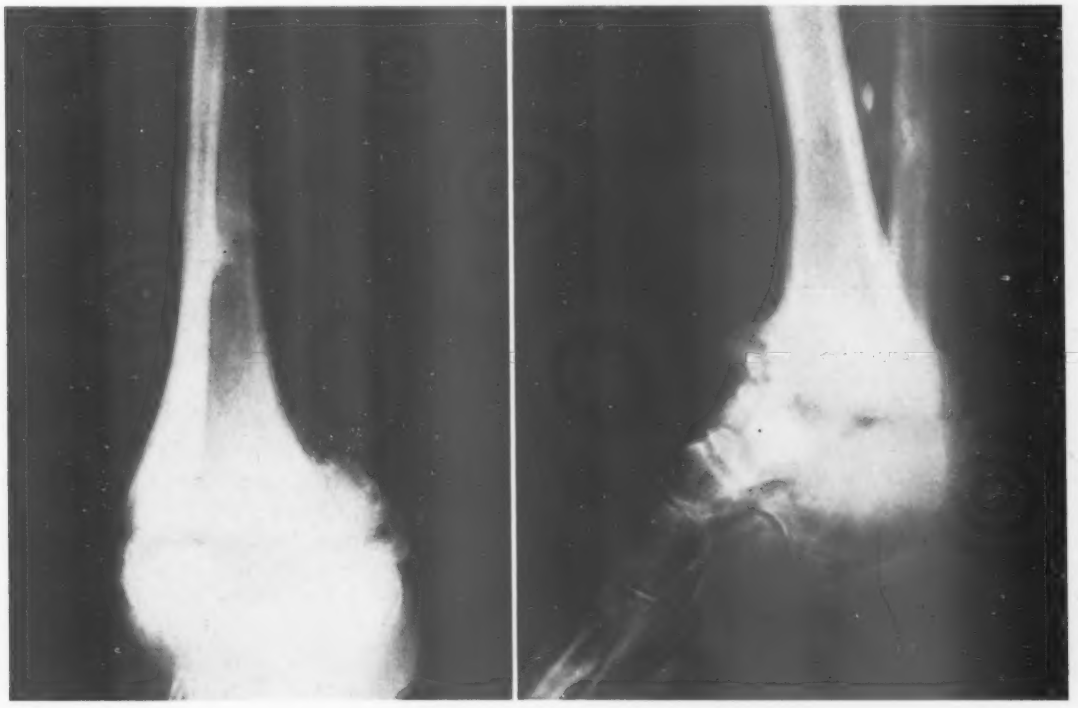

Fig. 3. Left ankle. Changes similar to those in the right hip and left shoulder are present.

Anatomical Changes. The onset is ordinarily insidious, the first symptom usually being periarticular swelling, unaccompanied by pain or other phenomena of inflammation. The disease advances rapidly with disintegration of the articular cartilages, soon followed by destruction of the underlying bone which becomes fragmented. Within a few weeks, the joint may become completely disorganized and flail-like. From then on, the destructive changes abate and proliferative changes begin. Villous and polypoid tabs appear in the synovial membrane. Numerous osteophytes, liberated by the destructive process, appear in the region of the joint and periarticular tissues and lay down new bone. This new bone formation is apparently ill-controlled as there rarely develops any firm union between the fragments of bone such as is ordinarily seen following a traumatic fracture. Small and large knobs and "stalactites" (Charcot's term) appear, thus giving the joint its characteristic irregular swelling and crunchy, grating feeling. The bony fragments retain all of their calcium, so that roentgen examination shows their density to be equal to, if not greater than, that of normal bone.

Occasionally following injuries of the spinal cord and in the course of tabes dorsalis, calcified osteoid masses may appear

FIG. 4. Left leg. Soft tissue exposures to show changes simulating myositis ossificans.

in the periarticular soft tissues, either in the joint capsule or ligaments or along the fascial planes. Some of these changes resemble closely those found in myositis ossificans. Israel[3] has reported a case of traumatic severance of the cord which was followed by marked bone formation about one hip joint and both knees with long spurs extending down the leg along the shaft of the tibia; he also has reported a case of calcification of the hip joint capsule following a gunshot wound of the spine in which the cord was destroyed, and several other cases of paraplegia in which there were abnormal calcium deposits in the collateral tibial ligaments, the knee joint capsule and the vastus femoris muscle. He also described a case of myelitis in which a shell of bone surrounded the sciatic nerve. None of these cases showed fractures or other changes similar to Charcot's disease. Israel believed that the abnormal calcification was the result of trophic changes and not of injury.

Läsker[4] cited a case of alcoholic polyneuritis in which ankylosis of both hips was produced by calcification of the joint capsules, and in which a lesser degree of calcification was present in the capsules of both knees.

Laux[5] reported the case of a patient, thirty-two years of age, with ascending paralysis, who developed calcification of the soft tissues about one hip joint and in the muscles of the lower femur six months following the onset of the paralysis.

The case reported below presents several unusual features. Simultaneous arthropathic lesions developed in the left shoulder, right hip and left ankle, all with marked disorganization of the involved joints. Subsequently, marked proliferative changes occurred in these joints with knob and stalactite formation, and changes resembling myositis ossificans appeared in the left leg and foot.

CASE REPORT

A. R., a divorced white male, aged forty-seven, was admitted to the Mary Fletcher Hospital on October 7, 1935. He had had two previous admissions, one in 1914 at which time a diagnosis of tabes dorsalis was made, and one in 1920 at which time a diagnosis of multiple Charcot's joints was made.

In 1912, he developed a penile chancre and was given mercurials and iodides for several months. No intravenous nor intramuscular therapy was employed and the patient abandoned all antisyphilitic therapy at the end of this time. About two years later he was given several courses of salvarsan and mercurials, during which time his blood serology was positive. During the next ten years, the patient had occasional short courses of salvarsan and mercury therapy. His blood Wassermann became negative in 1922 and has not been positive since that time. A spinal fluid examination in April, 1935, was negative; another in November, 1935, resulted in a slightly positive Wassermann reaction, with a colloidal gold curve of 0101100000.

In 1918 he received a traumatic fracture of the shaft of the left humerus which healed readily.

In 1920 the patient developed painless swelling and instability of the left ankle. The condition progressed rapidly and necessitated hos-

pitalization for several months. At about the same time the right hip became slightly swollen, but was not as troublesome as the ankle. Weight-bearing was readily accomplished on the right, but was difficult on the left, due to instability of the ankle joint. He was fitted to a brace for the ankle and with the aid of crutches was able to walk about and do light work. Since that time, the ankle and hip have become progressively more deformed; at night the patient was troubled by aches in his muscles and the joints were flail-like. During the past few years, he has had increasing difficulty in getting about in the dark, and on several occasions has fallen to the floor.

The important features in the physical examination are detailed below. Both pupils reacted to accommodation but not to light; the right was slightly smaller than the left. The left shoulder was slightly more prominent than the right and abduction was limited. Palpation of the shoulder revealed numerous small bony nodules in the region of the joint, and moderate widening of the upper humeral shaft, painless and non-tender. The chest was negative.

The abdomen was of normal appearance, except for slight prominence mesial to the right side of the pelvis. Deep palpation in this area disclosed a long, rib-like spicule of bone which extended upward from the hip joint to a point above the level of the iliac crest and just external to the bodies of the lower lumbar vertebrae.

The right hip was greatly enlarged, with loss of the usual bony landmarks. There was an upward dislocation of the hip on the ilium and palpation revealed the presence of numerous small smooth fragments of bone in and about the joint. Passive motions in all directions were greatly limited.

There was marked periarticular swelling about the left ankle with mushrooming of the lower tibia and inward displacement of the tarsal bones. Very little voluntary motion was present, and a loose, shucking motion was noted on manipulation.

All other bones and joints were negative. The knee jerks and ankle jerks were absent; deep vibratory sense was lacking over the left shoulder, lower trunk and both lower extremities. No paralyses were noted. A few enlarged glands were palpated in the left groin, but none elsewhere. Blood pressure readings, blood count findings, urinalyses, and blood phosphorus, calcium and phosphatase determinations were all within normal limits. The blood Wassermann was negative with both plain alcoholic and cholesterinized antigens. The spinal fluid Wassermann gave a slightly positive reaction.

Roentgen Findings. The left ankle, right hip and left shoulder joints showed advanced destructive changes in the articular ends of the bones with widespread fragmentation, and accompanied by marked proliferative changes. In the ankle, the process was largely confined to the lower extremity of the tibia which was completely disorganized, the bone being mushroomed to about three times normal width, and displaced externally. The bony fragments were of greater density than the bone of the right ankle. Many long spurs of bone extended into the soft tissues, one extending along the dorsum of the foot as far as the distal third of the shaft of the second metatarsal; several others extended upward along the shaft of the tibia. Several sharp spicules of bone took origin from the mid-shaft of the tibia and extended upwards to within a few centimeters of the tibial head. There was also a moderate increase in subperiosteal cortical bone on the anterior margin of the tibia.

In the right hip, the destructive process involved the head, neck and trochanters; the upper end of the shaft was dislocated upwards onto the iliac crest. A number of bony knobs had formed on the fragments of bone, and one long stalactite resembling a rib in outline and bony structure projected upward and inward to the level of the right transverse process of the third lumbar vertebra.

The left shoulder showed similar changes, with involvement of the head and upper neck of the humerus, with a resulting fungoid appearing mass of osteoid tissue in the region of the joint. The shaft of the humerus was greatly deformed, partially as the result of the old spiral fracture, and partially from osteophytic proliferation, so that it was about twice normal width and very irregular in outline.

Roentgenoscopic examination of the entire skeleton revealed no other similar lesions in bones, joints or soft tissues.

Comment. In view of the history of inadequately treated syphilis of more than twenty-three years' duration and of symptoms and signs of tabes dorsalis of twenty-one years' duration, and with a faintly positive spinal fluid serology, it is believed that a definite diagnosis of tabes can be

made in this case. The absence of history of spinal trauma, and the absence of the usual clinical symptoms and signs of syringomyelia seem sufficient to rule out these conditions.

The multiplicity of lesions with lack of bilaterality, the involvement of areas whose nerve supply is derived from widely separated cord segments, the marked destructive and marked proliferative changes about the joints, and the unusual deposits of calcium along the fascial planes of the foot and leg are all unusual features of this case.

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HODGKIN'S DISEASE AND ALLIED CONDITIONS OF BONE*

By RICHARD DRESSER, M.D., *and* JACK SPENCER, M.D.
BOSTON, MASSACHUSETTS

HODGKIN'S disease is primarily an affection of the lymphatic system which presents a characteristic microscopic picture and usually runs a well-known clinical course. There are several conditions which are clinically identical, but in which there is some variation in the histology. Under the latter group are included malignant lymphoma, lymphoblastoma, reticulum cell sarcoma, and lymphosarcoma.

The etiology of Hodgkin's disease and these allied conditions is unknown and pathologists differ as to classification. The presenting clinical picture in the majority of cases is enlargement of the lymph glands, frequently accompanied by enlargement of the spleen and liver. The disease often extends to structures outside the lymphatic system, and occasionally may be found in various tissues of the body without clinical evidence of lymph gland involvement.

In 1926 one of us reviewed 95 cases of Hodgkin's disease and found 4 with bone involvement, an incidence of 4.4 per cent. During the next five years an additional 149 cases were seen in which special attention was directed to the roentgen demonstration of bone lesions. In this second series there were 16 cases which showed definite osseous changes, an incidence of 10.7 per cent. In the next five year period we were able to collect an additional 46 cases of Hodgkin's disease in which bone changes were found ante mortem by roentgen examination. The diagnosis was established by biopsy or post-mortem examination in all instances. The sections of most of these cases have been carefully reviewed by Dr. Henry Jackson, Jr., and Dr. Frederic Parker, Jr. In a personal communication they have stated that the great majority belong in the Hodgkin's group, a much smaller percentage are classed as reticulum cell sarcoma, and only a few are lymphosarcoma. This work will be published in the near future.

Uehlinger places the incidence of bone involvement as high as 34 per cent, and Craver and Copeland have found osseous changes in 15.7 per cent. If those cases in which bone involvement is discovered at autopsy are excluded, one may expect to find roentgen changes ante mortem in approximately 10 per cent of all cases of Hodgkin's disease.

The greatest number of cases in our series were in the third and fourth decades. The youngest was eleven years of age, the oldest sixty-eight years. Both sexes were equally affected.

A total of 66 cases with 120 bone lesions has been observed to date. The distribution in this series in order of frequency is as follows: spine, 29 (lumbar 18, dorsal 8, cervical 3) (24.1 per cent); pelvis, 23 (19.1 per cent); femur, 19 (15.8 per cent); skull, 11 (9.1 per cent); ribs, 11 (9.1 per cent); sternum, 9 (7.5 per cent); clavicle, 4 (3.3 per cent); tibia, 4 (3.3 per cent); humerus 4 (3.3 per cent); scapula, 3 (2.5 per cent); os calcis, 1 (0.8 per cent); radius, 1 (0.8 per cent); maxilla, 1 (0.8 per cent). This follows closely the distributions given by Uehlinger with the exception that we have observed a greater number of cases with involvement of the extremities, especially the femur.

The roentgen picture usually simulates that of metastatic malignancy. It may, however, be confused with Ewing's tumor, osteogenic sarcoma, bone cyst, osteomyelitis, or other inflammatory bone conditions. In no case is the roentgenogram entirely characteristic.

* The material for this publication has been collected chiefly from the Massachusetts General Hospital, with the addition of a small number of cases from the Collis P. Huntington Memorial Hospital, the Palmer Memorial Hospital, and the Pondville Hospital at Norfolk (Massachusetts State Cancer Hospital).

Fig. 1. Destruction of the body of the first lumbar vertebra with preservation of the intervertebral space. The lesion simulates metastatic malignancy.

Of the 29 cases with involvement of the vertebrae, the process was destructive in all but two. As in metastatic malignancy the vertebral bodies were chiefly involved with preservation of the intervertebral spaces (Fig. 1). In 2 cases the changes were osteoplastic simulating the so-called "Elfenbeinwirbel" described by Hultén (Figs. 2 and 3). There may be mushrooming of the vertebral bodies giving rise to injury of the cord with paralysis.

In the pelvis the process is usually destructive. One generally finds large areas of bone erosion with sharply defined margins. Occasionally the margins are not well defined. In one case multiple, small punched out areas were observed which exactly simulated multiple myeloma (Fig. 4). The diagnosis in this case was not definitely established until after autopsy. Infrequently a purely osteoplastic picture is seen in the pelvis, or destruction and proliferation may exist together (Fig. 5). In one case, previously reported, the increased density of the bones of the pelvis simulated closely the osteoplastic changes seen in metastatic carcinoma of the prostate.

The changes in the extremities are much more variable than in the bones of the axial skeleton. The lesions usually occur in

Fig. 2. Osteoplastic changes in the fourth and fifth lumbar vertebrae, "Elfenbeinwirbel" (autopsy confirmation).

Fig. 3. Osteoplastic changes in the lower lumbar vertebrae and sacrum. Pain in the back was the first symptom of disease (biopsy of gland).

Fig. 5. Combined destructive and proliferative process in the ilium which gave rise to the presenting symptoms. The possibility of Hodgkin's disease was first suggested from the roentgenogram. Diagnosis confirmed by biopsy from a small inguinal gland.

Fig. 4. Multiple small, sharply defined areas of bone destruction simulating multiple myeloma (autopsy confirmation).

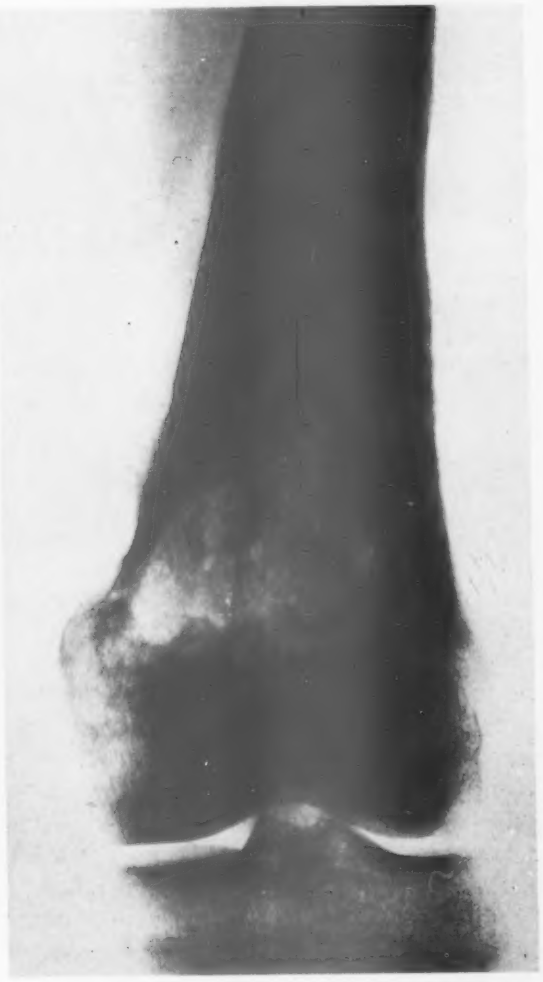

Fig. 6. Lesion of lower end of femur erroneously diagnosed primary bone tumor. There were no peripheral glands and no other bones involved. Diagnosis of Hodgkin's disease after amputation of the extremity.

FIG. 7. Circumscribed area of bone destruction in the mid shaft of the tibia simulating an inflammatory process. No peripheral glandular enlargement. (Biopsy from bone lesion.)

the ends of the long bones, most frequently in the femur. The mid portion of the shaft, however, may be invaded. The process is primarily destructive and originates in the medulla. There may be varying degrees of expansion of the cortex, erosion of the cortex, and periosteal proliferation. The picture may simulate a primary bone tumor, a bone cyst, or an inflammatory process (Figs. 6 and 7). In 2 cases there were spontaneous fractures (Fig. 8). In only one instance was a lesion observed below the wrist or ankle. In this case the patient developed pain in the heel and shortly after this a destructive process was observed in the os calcis by roentgen examination (autopsy confirmation).

The ribs and sternum are favorite sites for bone infiltration. In fact, our interest in this subject was first aroused by the appearance of large sternal masses in several cases under treatment for Hodgkin's disease at the Massachusetts General Hospital (Fig. 9). The process in the sternum is usually destructive, but there may be bone proliferation and expansion. In one case reported by Uehlinger, new bone was laid down in such a manner as to simulate the ray formation of osteogenic sarcoma.

We have observed only destructive changes in the bones of the skull. The areas are usually circular with sharply defined margins, but the borders may be ir-

FIG. 8. Cyst-like area in the shaft of the femur with spontaneous fracture. (Biopsy gland of neck.)

regular and ill defined. Frequently there is a soft tissue tumor directly overlying the area of destruction. In one case, previously reported, a soft tissue mass of this type on the scalp was the presenting symptom.

The shoulder girdle is involved in a small percentage of cases. In 3 instances there were small destructive areas in the scapula, and in 4 cases the clavicle was involved. In one case there was a cyst-like lesion involving the middle third of the clavicle with periosteal reaction. There was no clinical evidence of Hodgkin's disease and extensive roentgen studies demonstrated no other bone lesions. Diagnosis was made by biopsy (Fig. 10). In a second case, without clinical evidence of Hodgkin's disease, a single destructive lesion in the inner third of the clavicle was discovered, without changes in the other bones. This simulated the picture produced by syphilis so closely that antiluetic treatment was tried before the correct diagnosis was finally established by biopsy. In a third case a destructive lesion with spontaneous fracture in the outer end of the clavicle was discovered in a case of generalized Hodgkin's disease.

Bone involvement has usually been considered as a late manifestation of the disease; however, in our series of 66 cases there were 16 in which the bone lesions gave rise to the presenting symptoms; that is, the bones were involved early in the course of the disease in nearly 25 per cent. This will be discussed more fully in a separate paragraph dealing with lesions simulating primary bone tumor.

Fig. 9, *a* and *b*. Large sternal mass with bone destruction and proliferation.

Extension to the bone occurs in two ways: first, direct invasion from adjacent diseased nodes; second, a metastatic dissemination presumably via the blood

Fig. 10. Cyst-like area in the mid third of the clavicle. No other bone lesions. No enlargement of the peripheral glands. (Biopsy from clavicle.)

stream. A primary Hodgkin's disease of bone without involvement of lymph glands, spleen or liver has not been observed. Livingston has reported one case without lymph node involvement, but with evidence of disease in the spleen and liver.

According to Uehlinger the hematological dissemination of the disease may be characterized by a rapidly progressive anemia and leukopenia, the latter involving all the white blood elements. The blood changes are in part directly the result of infiltration of the blood-forming bone marrow. This is analogous to the rapidly progressive anemia often observed in the diffuse bone metastases of cancer of the breast. Invasion of the skull generally gives no clinical evidence other than the frequent appearance of a soft tissue mass directly over the area of bone destruction. Involvement of the spine almost invariably gives rise to pain which does not bear a constant relationship to the degree of bone destruction. Pain in the back may precede the roentgen demonstration of a spine lesion by several months. Lesions in the pelvic bones are often asymptomatic unless they are adjacent to the sacroiliac or hip joints when they nearly always give rise to pain. This pain may be referred down the lower extremity. Lesions in the sternum and ribs give rise to visible and palpable tumor masses and occasionally cause pain on deep inspiration. Involvement of an extremity usually gives rise to pain, particularly when the lesion is located close to a joint.

In a recent communication we have reported 3 cases of Hodgkin's disease of the extremities which were erroneously diagnosed primary bone tumor both clinically and roentgenologically. In the first case the evidence was so strongly in favor of a primary bone tumor that the extremity was amputated (Fig. 6). In the second case the correct diagnosis was made by biopsy of the bone lesion. This was followed by an infection which made amputation of the extremity necessary. The third case showed involvement of the upper end of the femur

Fig. 11. Destructive and proliferative lesion at the lower end of the femur diagnosed Hodgkin's disease from roentgenogram. No peripheral glandular enlargement. (Biopsy confirmation from bone lesion.)

which simulated Ewing's tumor. A diagnosis was made by biopsy of the bone lesion. A fourth case of this kind has subsequently been brought to our attention by the orthopedic department of the Massachusetts General Hospital.

A female, aged sixteen, came under observation with the complaint of pain and swelling in the right knee of eight months' duration. This pain was at times severe enough to keep the patient awake at night. Examination showed the region of the right knee and distal third of the right thigh to be moderately enlarged. There was no local tenderness. Flexion was moderately limited, but the leg could be fully extended. There was no enlargement of the peripheral lymph nodes; the spleen and liver were not palpable. The roentgen interpretation by Dr. Richard Schatzki was as follows: "The findings are those of a malignant tumor of the lower end of the right femur. I would place in order of probability: lymphoblastoma, first; Ewing's tumor, second; osteogenic sarcoma as a remote third; an inflammatory process is very unlikely" (Fig. 11). There was no roentgen evidence of involvement of other bones. A biopsy of the bone lesion was reported as reticulum cell sarcoma, and high voltage roentgen treatment was instituted. This case illustrates the importance of considering the possibility of Hodgkin's disease in any unusual bone lesion, even though the glandular manifestations are entirely absent.

The response of bone lesions to radiation treatment is exceedingly variable. Although striking regression of the disease is occasionally observed, the osseous foci are, on the whole, less radiosensitive than the glandular foci. The sternal cases have shown the most satisfactory response, and in a few instances we have observed regression of the disease in other bones. It has been our experience that potentials of at least 200 kilovolts are superior to the lower voltages. Small divided daily exposures of 200 to 300 r (measured in air) with total doses of 600 to 1,200 r per portal have been found to be fully as effective as larger doses, and this method possesses the advantage that the treatment may be frequently repeated. Relief of pain is very striking in many cases, and symptomatic improvement is frequently obtained even though there is no evidence of bone regeneration.

Although much can be done in a palliative way, the prognosis in Hodgkin's disease is grave. Thirty of the group of 66 cases with bone involvement have complete records extending from the time of the first symptom to the time of death. The average duration of life was three and a half years from the time of onset of the disease, and only eleven months after roentgen demonstration of bone lesions. The longest duration of life occurred in those patients presenting sternal tumors, 4 of whom lived five years or more.

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OSTEOPETROSIS

REPORT OF EIGHT CASES OCCURRING IN THREE GENERATIONS OF ONE FAMILY*

By CLARENCE N. McPEAK, M.D.
FITCHBURG, MASSACHUSETTS

THE condition known as osteopetrosis (marble bones; Albers-Schönberg's disease) has been reported at various times in the literature, and up to the present I have found 68 cases recorded.† To this number I wish to add 8 cases which occurred in three generations of one family, namely, a grandmother, her two daughters and five children of one of these daughters. A sixth child of this daughter does not have the disease. The other daughter has two children, both of whom are normal.

Other cases have been recorded in which the disease affected members of two generations of a family but, so far as I know, this is the first series reported in which the disease has involved three generations, and it is the largest series yet recorded as affecting the members of one family.

The etiology of the disease is unknown. Many hypotheses have been advanced but none will satisfy in all cases. Pirie[1] advanced the theory that the disease is caused by epiphysitis, but I cannot conceive of so widespread epiphysitis without the appearance of any symptoms; another factor that rules out this theory is that the metatarsal and metacarpal bones reveal the process early in both ends, whereas these bones have epiphyses at only one end. Whatever the cause, the disease is hereditary, as several cases have been reported in which members of the same family have been involved; the series reported here adds weight to this statement. However, the real cause of osteopetrosis in the first member of a family is not known. In the series reported here I believe that the disease began with the grandmother (Case 1) as the family has had the custom of recording important events, such as sickness, fractures, and so forth, in the family Bible, and search of this shows that no members of the family before the grandmother had more fractures than might be expected to be found in normal families.

In the cases reported in the literature, in some a mother and her children and in some a father and his children have been affected, so that it is known that the disease can be transmitted by both sexes and that both sexes are about equally affected.

McCune and Bradley[3] wrote an article in which they reviewed exhaustively all of the reported cases; they presented all the roentgenologic and laboratory observations, results of metabolism tests and the findings at necropsy and at biopsy. The results have never been constant concerning the chemical examination of the blood or other laboratory tests. The changes revealed by the roentgenogram are the most uniform, but even here there are wide variations.

Two distinct types or manifestations of the disease apparently may be present. In one type the disease begins during intrauterine life, and at the time of birth marked marbling of the bones and other manifestations of the disease, such as hydrocephalus, marked anemia, mental deterioration, and so forth, which usually cause a fatal end early in life, may be noted; for this reason I have called the group, in which such conditions are apparent, the malignant group. In the cases which fall into this group, the course is roughly parallel. In the other group, which I term benign, the picture is entirely different, as the disease begins somewhat later in life, progresses at a much slower rate, and has as its chief manifestation a history

† Since this paper was written another case reported by Stenström[2] has come to my attention.

* From the Department of Roentgenology of the Henry Heywood Memorial Hospital, Gardner, Massachusetts.

of frequent fractures which follow relatively mild trauma. Even this history of repeated fractures may be absent, and there may be no evidence of the disease; the condition may be discovered only on routine examinations of all members of a family in which there is a known case of marble bones. In the series reported here, all of the patients had the benign type of the disease, and it is with this type that this paper will deal.

The disease may appear at any time after birth when the epiphyses are still open. In most cases it appears within the first year or two of life. The age of the patient is no indication of the extent of the marbling, as some of the younger members of this series revealed more marked changes than some of the older members. The disease progresses constantly throughout the period of growth, and may even continue to progress slightly after this period.

In many cases the disease may be suspected before the roentgen examination because of a history of repeated fractures following relatively mild trauma. In many of the cases there may be no clinical evidence of the disease except for the roentgen observations. In fact, the condition in the cases here reported was discovered accidentally. The first patient had a roentgenogram made because of a fracture of a clavicle resulting from a bad fall; there was sufficient trauma to fracture a normal bone. The discovery of the condition resulted in a check up of all of the living members of the family, with the exception of the father of 5 patients (Cases IV to VIII, inclusive). In only 2 cases in this series was there a history of repeated fractures following mild trauma, although this is supposed to be a characteristic of this disease. One patient (Case I) has had repeated fractures of both hips, and as a result she was afraid to move about much in her later years, as she was in constant fear of refracturing a hip; for that reason it was with considerable difficulty that roentgenograms were obtained of her. The second patient (Case II) has had no fractures. The fourth patient (Case IV) has had repeated fractures of the hip and of one humerus. The fifth patient (Case V) has had no fractures. The first member of the family (Case VI) to come under my observation has had a fracture of the clavicle, and recently fractured both bones of the lower leg as a result of a bad fall when skiing. Both of these fractures were the result of trauma sufficient to cause a fracture of a normal bone. The other 2 patients (Cases VII and VIII) have had no fractures. The ages of the patients in this series ranged from eleven months to seventy-two years (Fig. 1).

Anemia of variable degree, with enlargement of the liver, spleen and lymph nodes, has been reported as a fairly constant observation; this is thought to be due to obliteration of the medullary canals by the deposit of the excess calcium. Only a very slight degree of anemia is present in any of the patients in this series, the concentration of hemoglobin varying from 75 to 85 per cent; in only one case was this less than 80 per cent, the erythrocyte count varying from 4,070,000 to 5,080,000, with only one case in which the count was less than 4,500,000. There was no enlargement of the liver, spleen or lymph nodes in any of the patients in this series.

The following observations have been noted in the other cases reported: impairment of mentality, hearing and vision; less than the usual amount of pain following fractures, and elevation and thickening of the periosteum. In the series reported by me, all of the patients were normal mentally, had no impairment in vision or hearing, and had the usual amount of pain following fractures. There had been no elevation or thickening of the periosteum.

Kerr[4] has recently reported the case of a negro with marble bones who also had an osteogenic sarcoma of the femur. There had been no symptoms of marble bones, and the condition was discovered at the time of examination of the femur. This patient had a large head, and it was noted that his father also had a large head, but roentgenograms had never been made of any

other members of the family. If roentgenograms had been made, more cases of the disease might have been found, and more proof added to the theory of heredity. As Kerr pointed out, this is the only known case occurring in a negro, as all others were found to have occurred among white people.

The time of appearance of ossification in the epiphyses and their time of closure has not been affected by the disease. In one case (Case VII) in this series, there was delay in ossification in the epiphyses, but it is known that this patient suffers from hypothyroidism. At the time of her last examination, however, the ossification had reached normal proportions for her age.

The disease progresses slowly in some cases and more rapidly in others. The medullary canal is apparently narrowed in the affected regions, and in the denser regions it cannot be seen. This is thought to be more apparent than real and to be caused by the excess of calcium deposited in the cortex, thus preventing the roentgen rays from penetration sufficient to show the canal. If the canal were obliterated as much as it appears to be, then the patients would be definitely anemic and would have an enlarged liver, spleen and lymph nodes, whereas none of the patients in this series had these anomalies.

The earliest reported sign of the disease has been a narrow dense line in the diaphysis at the epiphyseal edge of the humerus, femur and tibia; soon afterward this appears in the other bones. This line has been described as flaring at the edges. I do not agree that this is a sign of marble bones. It is true that it is seen in this disease, but it is also seen in many normal children. The earliest real sign of the disease is slight increased density of the bone just below this line, which gives it a somewhat dense appearance similar to that of ground glass. As it extends down the shaft the bone above increases in density, and the trabeculae are entirely obliterated; as the disease progresses down the shaft, the bone in the upper end becomes so dense that the

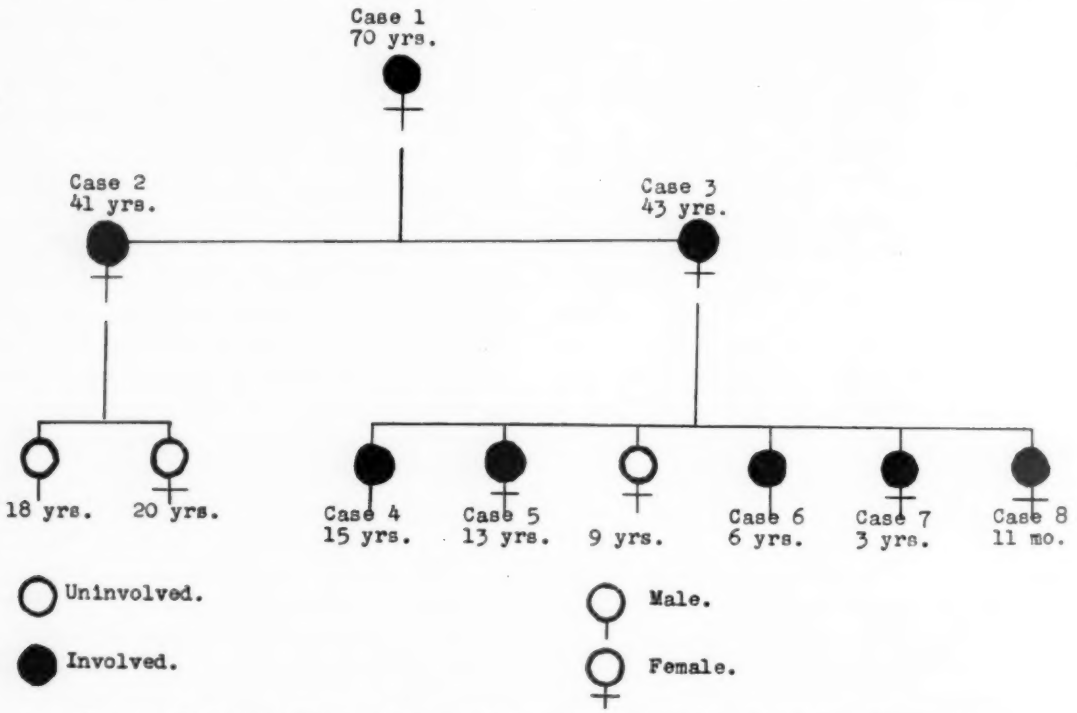

FIG. 1. This chart indicates the age of the patient at the time of the first observation.

medullary canal becomes invisible. There is no sharp line dividing the three stages as one fades into the other, and the lower edge of the process fades into the normal bone.

Soon after definite involvement is seen in the diaphysis the process crosses the epiphyseal line and the center of ossification quickly becomes uniformly dense and remains so. In the lower ends of the radius and ulna may frequently be seen narrow dense transverse bands of bone, between which there may be normal bone or bone revealing only slightly increased density. This observation has been described as typical of the disease, but in this series it is very inconstant, and unreliable as a pathognomonic sign. These bands may practically disappear as the patient becomes older. In one case (Case VI) dense vertical lines were noted, running from the articular surface of the lower end of the femur up the shaft for about 3 inches (7.6 cm.), but this is the only case in this series in which this was noted, and I have not seen it reported in other cases.

The process begins in the lower end of the radius as it does in the other bones, but later the radius may give evidence of actual regression of the process, whereas the process increases in other bones. In one case there was also some regression in the bones of the foot.

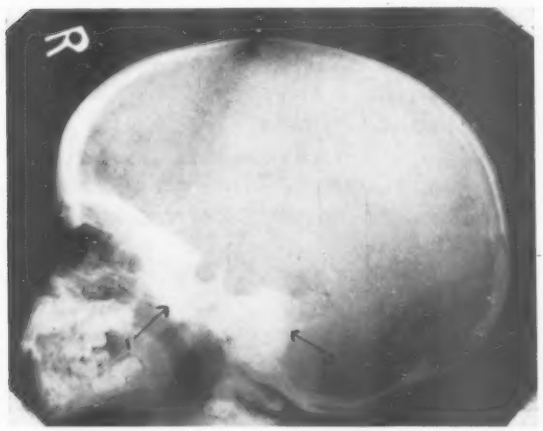

FIG. 2. Case VII. Observed in May, 1931, at the age of four. Arrow 1 points to marked increased density beneath the sella turcica. This is a very early finding in this disease. Arrow 2 points to marked increase in density of the temporal bone with obliteration of the mastoid cells. There has been no impairment in hearing.

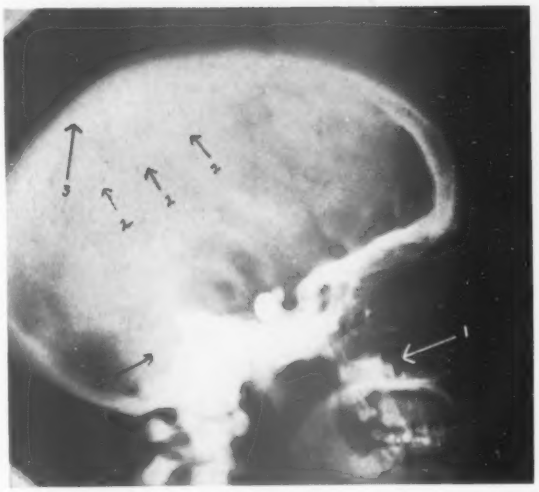

FIG. 3. Case IV. Observed in May, 1935, at the age of twenty. The late changes in the disease may be noted. Arrow 1 points to increased density in the maxilla; arrow 2 to increased density in the calvarium but with some of the diploe still visible; arrow 3 to increased thickness of the skull, and arrow 4 to obliteration of the mastoid cells. The marked density of the upper cervical vertebrae and beneath the sella turcica can be noted.

A typical finding has been a definite increase in the diameter of the femur, which begins at the juncture of the middle and lower third and extends to the supracondylar region, at which point the bone returns to the normal diameter. An increase in diameter may also be noted in the lower end of the tibia.

In some cases the process has been seen to involve even the sesamoid bones of the foot. Except in one case, studies of the chemical constituents of the blood have not been made, because the patients lived far from the nearest hospital which was equipped for detailed studies. One patient (Case IV) has been at the Beth Israel Hospital, Boston, where extensive examinations were made, but no significant variations from the normal were discovered. The details of this case will be reported from the hospital in a separate paper.

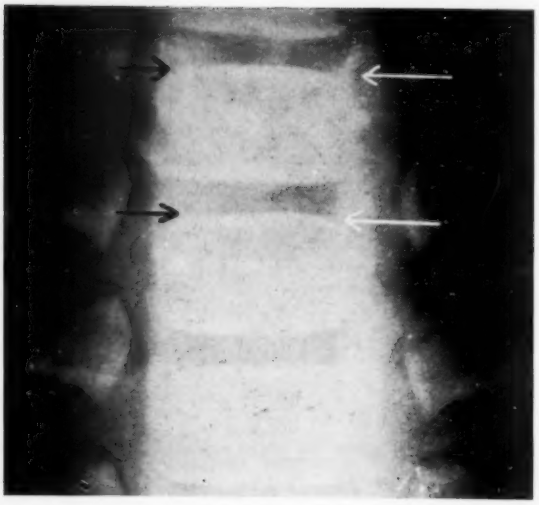

Fig. 4. Case VIII. The narrow dense line of increased density is the earliest manifestation of the disease in the bodies of the vertebrae. This occurs along the superior and inferior borders of the bodies.

The observations in the various bones are as follows:

Skull: There was marked thickening of the anterior and posterior clinoid processes and the floor of the sella, which extended into the wings of the sphenoid. Early in the disease the posterior sphenoid sinus becomes obliterated by the dense bone, and as the disease progresses this dense bone becomes thicker until almost the entire sinus will be obliterated. At this time there is beginning obliteration of some of the ethmoid cells. The mastoids may become involved. The first change is the appearance of dense bone around its periphery which soon invades the mastoid cells, causes them to become less distinct and finally to disappear completely. Even at this stage there is no impairment of hearing. The process may stop at any stage, and does not necessarily progress until the mastoid is obliterated. The final change in the skull is increased density of the calvarium, with thickening of the bone and obliteration of the diploe. In none of these cases has the process caused any appreciable enlargement of the cranium, and none has had the extensive involvement observed in some cases reported, particularly in the case reported by Kerr.

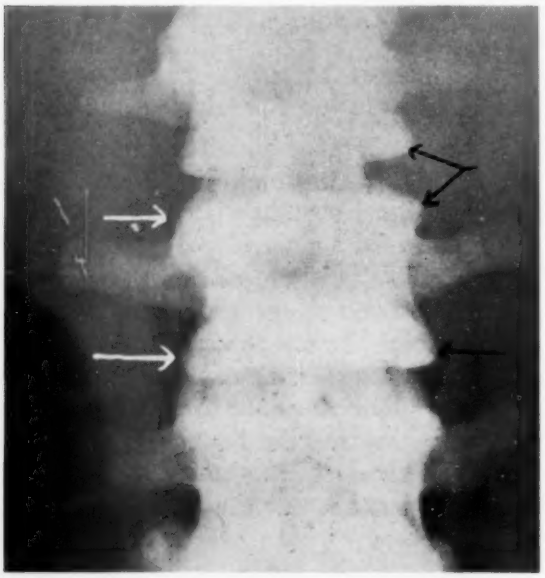

Fig. 5. Case V. Observed in May, 1935, at the age of seventeen years. Anteroposterior view, which reveals later changes in the vertebrae.

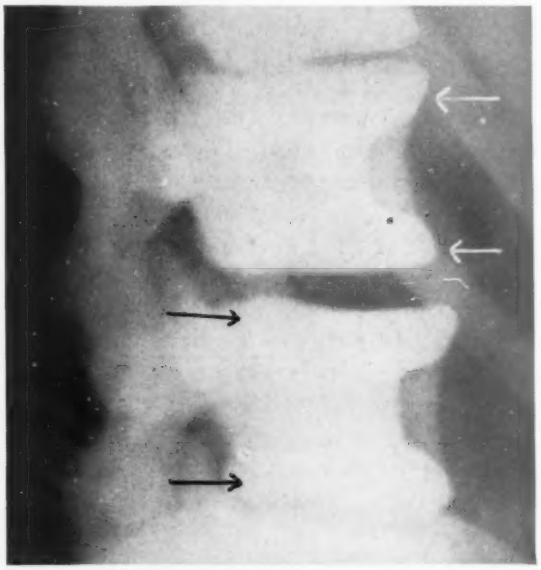

Fig. 6. Case III. Lateral view which reveals the later changes in the bodies of the vertebrae.

Spine: The entire spine was involved; the sacral and coccygeal segments revealed the least changes. The bodies of the vertebrae revealed a dense band along the superior and inferior margins, and as the disease progressed these bands became thicker and approached the center. The bone between revealed some increase in density which was not as marked as that in the inferior and superior borders, so that they have somewhat of a dumb-bell shaped

appearance. The spinous and transverse processes were also involved.

Ribs: The earliest change was a diffuse, ground-glass appearance caused by the increased density, and this was soon followed by complete obliteration of the trabeculae. This is not a uniform process here as the dense bone may occur as islands which extend along the course of the rib and may be surrounded by normal bone. These islands may be only 1 or 2 cm. in length, or may extend for almost the entire length of the rib.

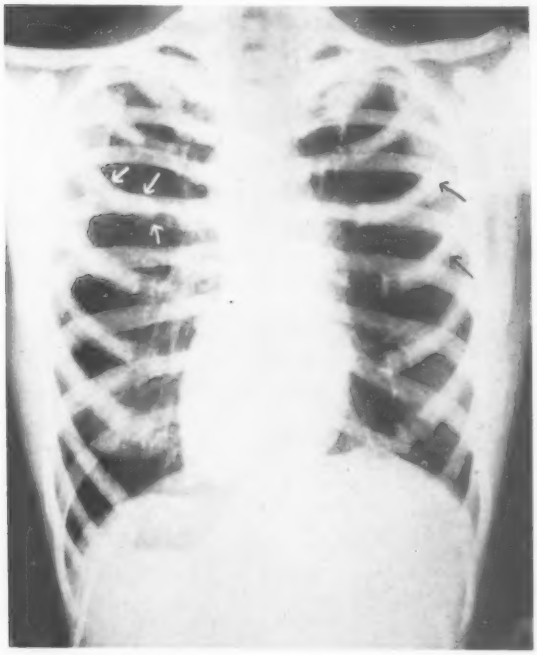

Fig. 7. Case III. Arrow points to "islands" of dense bone in the anterior ribs. The greater density of the anterior ribs when compared with the posterior ribs can be seen.

Shoulder girdle: The scapula gave evidence of the greatest involvement at the acromion process, around the glenoid and the neck, and revealed less involvement in the wing and coracoid process. The clavicle revealed almost completely uniform increase in density for its entire length.

Humerus: The early changes in this bone have been described previously. After the process has extended several centimeters down the shaft, the lower end of the bone begins to reveal involvement, but here it progresses much slower and in the most advanced case in this series it did not extend up the shaft for more than 1 or 2 cm. from the lower end of the bone.

Fig. 8. Case III. Observed in May, 1935, at the age of forty-eight. Arrows point to areas of decreased density which may be noted in several cases of this series.

Forearm: The upper ends of the bone revealed only slight involvement, while the lower ends evidenced the most marked changes. However, in none of this series had the process extended beyond the ground-glass stage, and the trabeculae remained visible. Narrow dense bands may be seen in both ends of these bones, which extend across the width of the shafts with normal or less involved bone between the bands. As the patient grows older the bone in the lower ends of the ulna and radius loses much of its increased density, and returns more to its normal appearance.

Fig. 9. Case I. Observed in August, 1931, at the age of seventy. Marked increased density of all of the bones and marked deformity of both hips due to previous repeated fractures may be noted.

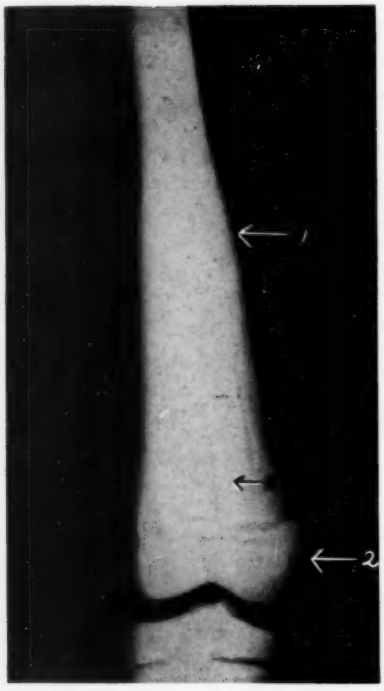

Fig. 10. Case vi. Observed in May, 1935, at the age of thirteen years. Arrow 1 points to increased diameter of the bone; arrow 2 to alternate bands of increased and decreased density in the epiphysis, and arrow 3 to dense vertical bands running up the shaft of the lower third of the femur. (These bands show much more clearly in the original films.)

Wrist and hand: The earliest change seen in the carpals was a narrow dense line extending around the periphery. As the disease progresses this band becomes thicker and encroaches on the center, but in no case does the entire bone become dense. This change is very typical of the disease.

Pelvis: The bones of the pelvis revealed a gradual increase in density until they were completely involved. The earliest changes were found along the roof of the acetabulum. The ischium and pubic bone revealed the least changes. One peculiar but characteristic observation has been a rough crescentic band of increased density, but in some cases the band which runs across the ilium parallel to the crest may be of decreased density. This is always bilateral.

Femur: The changes were similar to those seen in the humerus, and the process began here at about the same time as in the humerus. The lower end, however, revealed more marked changes than the lower end of the humerus, but the process was not as extensive as in the upper end of the bone. In advanced cases there is an actual increase in diameter of the shaft, starting at the juncture of the middle and lower thirds, continuing downward and returning to the normal diameter at the level of the upper border of the condyle.

In one case narrow dense vertical bands were seen to extend from near the lower epiphysis up the shaft for about 3 inches (7.6 cm.) (Fig. 4).

Lower leg: The process here had advanced about as rapidly up the shaft as it had downward. The tibia revealed more marked changes than did the fibula. The lower end of the tibia may show an actual increase in the diameter of the shaft, as was noted in the lower end of the femur. These two bones are the only ones that revealed this change.

Foot: The changes noted were similar to those noted in the wrist and hand, except that

Fig. 11. Case viii. Observed in May, 1935, at the age of four years. Arrows 1 and 2 point to early involvement of the astragulus and os calcis; arrow 3 to early involvement of the lower end of the tibia, and arrow 4 to more extensive involvement of the upper ends of the tibia and fibula.

they were more extensive in the foot. The changes in the astragalus occur early in the disease, and may be of use in the differential diagnosis of osteopetrosis and lead poisoning. Some of the sesamoid processes also revealed increased density caused by involvement.

DIAGNOSIS

It is practically impossible to make the diagnosis of marble bones early in the course of the disease, unless its presence may be suspected because some other member of the family has the disease. In its earliest stage it is difficult to distinguish it from lead poisoning, but if roentgenograms are taken of the foot and skull, the differential diagnosis can probably be made as the astragalus and sphenoid reveal evidence of marble bones very early in the disease, whereas in lead poisoning there will be no changes in these bones. When it is remembered that marble bones always involves almost all of the bones of the body, then the diagnosis is relatively easy.

There is no real similarity between this disease and the changes found in the bones in osteosclerotic anemia, and there should be no trouble in distinguishing between the two diseases.[5]

PROGNOSIS AND TREATMENT

The disease constantly progresses, but the rate is slower after the epiphyses have closed. In the "malignant" type the prognosis invariably is grave, but in the "benign" type the patient may live to old age without any symptom of the disease ever developing, or may have frequent fractures following mild trauma and may never have any other symptom. No known treatment is effective.

REPORT OF CASES

Case 1. A. W., female, aged seventy, married, was seen in August, 1931. Only one roentgenogram was obtained, that of the pelvis, upper ends of both femurs and the lower three lumbar vertebrae. The bodies of the vertebrae revealed uniform marked increase in density. The spinous processes, the lateral masses and the transverse processes of the fifth lumbar vertebra had markedly increased density, but the transverse processes of the third and fourth lumbar vertebrae had no increase in density. Both ilia, ischia and the pubic bones had markedly uniform increase in density. The sacrum and coccyx revealed similar changes, but these were least marked in the lower sacral and coccygeal segments. The necks of both femurs revealed the result of repeated fractures with absorption and shortening, with no bony union on the left side, and with questionable union on the right side. The shafts, as far as might be seen, were markedly increased in density, but with superimposed atrophy, and the medullary canals were visible but greatly narrowed. There was calcification of the blood vessels of the pelvis and of the femoral arteries.

In this case, the extent of the marbling process is the most marked of any in this series. No examinations of the blood were made as the patient was not under my observation.

Fig. 12. Case vi. A more advanced stage of the disease may be observed. The changes in the tarsals and metatarsals are very characteristic of the disease. Arrow 1 points to the narrow rings of increased density in the os calcis; arrow 2 to unequal involvement of the anterior and posterior halves of the astragulus, and arrow 3 to the increase in the diameter of the lower end of the tibia with some increase in density of the bone but with more marked density in the epiphysis.

It was with much difficulty that the patient was finally brought in to permit the roentgenogram to be made. She was extremely apprehensive about being moved as she feared another fracture of the hip as several had occurred in the past following relatively mild injuries. She died in the early part of 1935 at the age of seventy-four.

Case II. U. B., female, aged forty-one, married, was seen in August, 1931. A roentgenogram of the pelvis of this patient was all that was available. The marbling was much less marked than that of her mother (Case I), and also less marked than that in some of the following cases in which the patients are much younger than she. The bodies of the fourth and fifth lumbar vertebrae revealed only slight involvement. The body of the first sacral segment was very dense. The wings of the sacrum gave evidence of increased density only along the first sacral ridge, and the coccyx was but slightly changed. The ilia revealed increased density along the sacroiliac joints, and extending downward involved the acetabula, ischia and ascending rami of the pubic bones. There was a crescentic band of increased density from 2 to 7 mm. in thickness that extended across the ilia and ran parallel to the crests and about 4 cm. below them. The heads, necks and upper ends of the femurs revealed an increase in density, but the trabeculae were still visible and the medullary canal was only slightly narrowed. In each of the greater trochanters there was an area of rarefaction 1 cm. in diameter, which was surrounded by a dense wall of bone from 2 to 3 cm. in thickness. There were similar but larger areas in the heads of the femurs or in the acetabula; the exact site could not be determined on the flat roentgenogram. There was marked calcification of the iliolumbar ligaments, but no calcification of the blood vessels of the pelvis. Examinations of the blood were not available in this case.

The patient had had no fractures and no symptoms referable to the disease. She has one son and one daughter, both of whom are almost adults, neither of whom reveal any evidence of the disease.

Roentgenograms of these two patients were made for me through the facilities of the Norwich Hospital, New York, and the courtesy of Dr. F. E. Roper of that city, as these two patients lived there and were never seen by me. I have seen all the remaining patients whose cases are reported, and I have followed their condition for more than five years.

Case III. A married woman, aged forty-three, was first seen in 1930. This patient is the daughter of the patient reported as Case I, the sister of the patient reported as Case II, and the mother of the remaining patients whose cases are reported. A roentgenogram of the thorax was all that was taken at that time.

Extensive marbling of the low cervical, the entire dorsal, and the upper three lumbar vertebrae was present. All of the ribs revealed the disease to some degree. Some of the ribs had uniform involvement, whereas others revealed islands of dense bone several centimeters in length, which may or may not have extended across the diameter of the bone, and which were surrounded by normal bone. Most of the ribs had large areas of normal bone. Both clavicles and the upper ends of both humeri were very dense. The coracoid process, neck and around the glenoid were markedly involved, but the acromion and the wing of the scapula revealed very little change from the normal.

In May, 1935, the patient was re-examined more thoroughly. The thorax revealed no appreciable change since the former examination. The heart was small, the total transverse diameter being only 40 per cent of the internal diameter of the thorax.

The calvarium revealed increased density in its upper half, and in this area there was actual increase in the thickness of the bone and the diploe were obliterated. Marked increased density was noted in the entire sella which extended into the wings of the sphenoid. The posterior third of the sphenoid sinus was obliterated by the dense bone. The mastoids were involved around the antrums, but the outlying cells were normal. Both mandibles revealed a slight increase in density in the dental area.

The entire spinal column revealed a marked increase in density of the bodies and transverse processes.

The entire pelvis revealed increased density. Crescentic bands of decreased density, similar to those described in the foregoing, were noted in the ilia and also in the pubic bones.

The upper and lower thirds of the femurs were very dense. The middle third is not shown on the films. The upper two-thirds of the

humeri were very dense, and the medullary canals were not visible. There was only slight increase in density of the condyles of the humeri and the trabeculae were not obliterated. The neck of the radius had a band of increased density 1 cm. in width that extended across the shaft. There was only slightly increased density of the upper end of the ulna. The lower end of the radius had indefinite narrow bands of increased density that extended across the diameter of the bone. The medial cortex of the ulna was thickened and the medullary canal was narrowed. The carpals revealed slightly increased density as did all of the metacarpals and phalanges.

The lower ends of the tibiae had several bands of increased density, from 1 to 3 mm. thick, that extended across their diameters. The trabeculae were not obliterated. The superior surface of the astragalus had a density of about 1 cm. in thickness, and extending from this were several narrow dense bands which encircled the bone and were about 1 to 2 mm. apart. The same conditions were present in the os calcis. These rings came very close to the periphery of the bone except in the posterior part where they were about 2 cm. from the periphery. Some of these bands described complete circuits while others formed arcs. The metatarsals and phalanges showed slight involvement. The sesamoids of the distal end of the first metatarsal were very dense.

There was some calcification of the blood vessels of the pelvis and lower extremities.

Erythrocytes numbered 4,070,000; the concentration of hemoglobin was 75 per cent.

The patient fractured a rib a few months ago following an injury, but had had no other fractures and no other symptoms of the disease.

Case IV. E. K., a boy, aged fifteen, was first seen in 1930. As with Case 1, this was another typical case of the disease, in that the patient had had numerous fractures following relatively mild trauma.

The skull revealed marked density of the anterior and posterior clinoid processes on the floor of the sella and extension into the wings of the sphenoid. The posterior half of the air space beneath the sella was obliterated by dense bone. The sella was apparently narrowed. The mastoid cells were obliterated by the dense bone. The other bones of the face, the skull and the mandibles revealed no evidence of the disease.

The entire vertebral column revealed marked increased density but this was less marked in the lower sacral and coccygeal area. All of the ribs showed marked diffuse involvement. There were no "islands." The posterior third of the ribs gave evidence of less density than did the remainder. The scapulae revealed general involvement, but this was less in the acromion and wing. The upper ends of the humeri, which may be noted on the film, were very dense. The epiphyses had not entirely closed. The lungs were normal and had not an unusual number of calcified glands. All of the bones of the pelvis revealed marked uniform involvement. There was a crescent-shaped band of decreased density 3 mm. wide that ran parallel with the crests across both ilia and about 4 cm. below the crests. In the upper ends of the femurs the bone was so dense that the medullary canal could not be seen. A solidly healed fracture of the left femur just below the trochanters was noted. There was some bowing of the shaft as a result of the healing of this fracture. The shaft of the left femur was 3 mm. wider than the right, but this was probably a secondary change due to the bowing. The epiphyses of the head and both trochanters were open, and the bone on both sides was equally involved.

Twelve days after this examination the boy was admitted to the hospital, with another fracture of the left femur at the site of the previous fracture. This united solidly in normal time.

One year after the first examination, March, 1931, the boy was re-examined. The filling of the sphenoid beneath the sella had progressed until only the anterior third was aerated. The ribs, clavicles and scapulae showed little change. The fracture of the femur had healed and only a little bowing resulted. The left elbow and both knees were examined at this time. The lower 3 cm. of the humerus had increased density on both sides of the epiphyseal line. There was slight increased density around the joint surface of the olecranon process, but there was no other involvement of the upper end of the ulna. The upper 3 cm. of the radius was visible and revealed alternate bands of dense bone and normal bone. The lower dense band was 5 mm. wide and involved only the medullary canal. The middle thirds of both bones of the forearm revealed slight diffuse increased density. The lower ends of the femurs and the upper ends of the tibiae and fibulae had narrow dense bands superimposed on the dense bone,

and running parallel to each other across the diameter of the bones. These bands were 1 mm. thick and about 5 mm. apart.

In December, 1932, the boy sustained an oblique fracture of the middle third of the left humerus. There was extensive marbling of the upper two-thirds of the humerus, and the fracture occurred in the lower end of the dense bone. This fracture united in normal time. The epiphyses were still open.

Roentgenograms taken in February, 1933, revealed very little change. The fracture of the humerus had healed almost solidly, only a faint line being partially visible across the shaft. An intercondylar fracture of the elbow was seen, with some periosteal reaction. This may have occurred at the time of the fracture of the shaft, as the former roentgenograms did not include the elbow.

In August, 1933, there was another fracture of the left femur at the site of the previous fractures. This united in normal time.

In December, 1934, the patient sustained an intercondylar fracture of the left humerus. This was at the exact situation of the previous fracture. The bone revealed little change since the last examination. Both condyles had dense bone which almost surrounded the olecranon fossa, but the cortex here was not involved. For about 10 cm. above this the shaft was apparently normal, at which point the marbling from above may be seen.

All of these fractures have followed relatively minor trauma. The usual symptoms of a fracture have been present and there has been no delay in union. This patient was admitted to the Beth Israel Hospital, Boston, for studies of the blood several months ago, at which time no definite variation from the normal was found, but these results will be published in a communication from that institution.

In 1935, re-examination of the patient revealed very little change in the spine, thorax, or extremities. The skull at that time revealed definite thickening of the bones of the vault. The mastoids were completely obliterated. The sella appeared to be very small, and the dorsum sellae was about 6 mm. thick. The shafts of the femurs, beginning at the juncture of the lower and middle thirds, had an actual increase in the diameter of the bone, and this progressively increased as it approached the condyles. Union of the epiphyses had progressed normally.

A lateral view of the spine was taken for the first time; this showed a very dense band of bone 1.5 cm. thick along both the inferior and superior surfaces of the bodies with the bone between denser than normal but not nearly as dense as these areas. This gives the bodies somewhat of a dumb-bell shaped appearance. May 30, 1935, the erythrocytes numbered 4,740,000 and the concentration of hemoglobin was 85 per cent.

CASE V. E. K., a girl, aged thirteen, was seen in April, 1931. The skull revealed involvement of the sphenoid and mastoids. The mastoids had not been obliterated. The marbling was not nearly as marked as in Case IV. The ribs revealed considerable involvement, which was most marked in the anterior halves. The heads and necks of the ribs were dense, and there were islands of dense bone near the spine. Both clavicles were involved and the scapulae revealed the greatest change in the coracoid, the neck and around the glenoid. The spine, pelvis and upper femurs had uniform changes. The same crescentic areas of decreased density were seen in the ilia, but here they were about 5 cm. below the crests. The epiphyses were normal. The ulna revealed slight increased density in the lower 5 cm. but the trabeculae were still visible. There was a band of dense bone 5 mm. in width extending along the diaphyseal side of the lower epiphysis of the radius. The center of ossification revealed a narrow band along the epiphyseal and joint surfaces. The carpals had a dense ring around their circumference. The tarsals revealed these changes to a more marked degree. The metacarpals and phalanges had only a narrow dense line on both sides of the epiphyseal line.

Re-examination of the patient in 1935 revealed a slight but definite increase in density of the vault, the sella, the greater wings of the sphenoid and both mastoids. The mastoid cells were not obliterated as they were in the preceding case. The thorax revealed only slight change. The vertebrae had the same dumb-bell shaped appearance. The upper two-thirds of the humeri were very dense and the medullary canals were invisible in this area. The bones of the hand and forearm had very little evidence of the disease. The dense bands noted previously had disappeared except for a narrow, wavy, indefinite line in the lower end of the radius. The lower thirds of the femur and the upper thirds of the tibiae revealed marked density. The same increase of diameter in the

lower shaft of the femur may be seen, and this also decreased to the normal diameter just above the condyles. Erythrocytes numbered 4,520,000, and the concentration of hemoglobin was 80 per cent.

Case vi. R. K., a boy, aged seven, was first seen in 1929. This patient was the first of the family to be seen. He was brought in because of a fractured clavicle. The changes seen on this roentgenogram led to the examination of the entire family.

The marbling in this case was much more advanced than that noted in Case v, and this patient was five years younger. The skull had marked density beneath the sella. There was markedly increased density of the bone of the posterior and the anterior clinoids, the floor of the sella, and this extended into the wings of the sphenoid. The air space beneath the sella was almost obliterated. There was questionable beginning involvement of the ethmoid cells. The mastoids revealed increased density but the cells had not been obliterated. There was a questionable increase in density of the vault. The entire spine revealed markedly increased density, and as in the other cases the lower sacral and coccygeal vertebrae revealed the least change. There was some extension of the condition into the transverse processes, but this was not as marked as in the spinous processes or the lateral masses. Both clavicles and the ribs revealed increased density for their entire lengths, but the medullary canals were still visible. The acromion, coracoid and neck of the scapulae were quite dense. The wing had less marked density but this was greater than normal. The upper 10 cm. of the humeri were visible and uniformly dense. The medullary canal was visible but appeared narrowed. The epiphyses were normal. All of the pelvic bones were dense except for the centers of the ilia. The upper 20 cm. of the femurs were visible and very dense. The density decreased slightly lower down the shaft. The lower ends of the ulna and radius revealed increased density, but the trabeculations were still visible. The ossification centers of the ulna and radius and three of the carpal bones revealed the "rings" but the other four carpals were normal. The metacarpals and phalanges had changes similar to those noted in the other cases. The bones of the foot revealed changes similar to those in the hands. The astragalus was 4.6 cm. long. The anterior wall of the ring of dense bone was 7 mm. thick and that of the posterior wall was 2 cm. The superior and posterior borders revealed the most marked changes.

Thirteen months later all of the bones revealed extension of the process. The ring shadows in the carpals and tarsals were thicker. The astragalus was then 5 cm. long, and the anterior wall of the "ring" 1 cm. thick and the posterior wall 3 cm. thick.

Examination in 1935 gave evidence of no appreciable change in the skull and thorax. The increased density formerly at the diaphysis of the radius was about 4 cm. up the shaft, with a narrow, slightly dense line at the diaphysis, the bone between being normal. There has been no increase in the process in the hands or feet, and instead there was some actual decrease in density and the bone had more normal appearance. The lower half of the femur revealed increased density and here were noted long, dense vertical bands that extended up the shaft from the epiphysis for about 3 inches (7.6 cm.). The internal condyles had several dense concentric bands forming partial rings. The lower half of the shaft had definite increase in the diameter of the bone. Erythrocytes numbered 5,000,000 and the concentration of hemoglobin was 80 per cent.

Case vii. U. K., a girl, aged three, was first seen in May, 1930. Only one roentgenogram was taken at that time, and that extended from the shoulders to the lower third of the femurs. The entire spinal column revealed increased density. There was some increased density in the ribs, but the trabeculations were still visible. The upper ends of the humeri revealed a band of dense bone 8 mm. in width along the diaphysis, with lipping of this area. The center of ossification was dense. There was a band of dense bone 1 mm. in thickness at the lower end of the humerus. The upper ends of the ulna and radius revealed no involvement. The changes in the pelvis were most marked in the roof of the acetabulum. There was a band 3 mm. in width along the diaphysis of the upper end of the femurs, and the shaft downward for 4 cm. gave evidence of increased density; the medullary canal was indistinct in this region. Ossification in the epiphyses was markedly delayed. The head of the humerus was 7 by 10 mm. in diameter, and the head of the femur was 5 by 2 mm. This patient was seen at the Children's Hospital, Boston, soon afterward, and a diagnosis of hypothyroidism was made.

Ten months later, in April, 1931, more roentgenograms were taken. The skull gave evidence of the most marked marbling of any patient of this series. Density was markedly increased in the anterior and posterior clinoids, on the floor of the sella and extending well out into the wings of the sphenoid. The air space beneath the sella was obliterated except for a small area anteriorly. The mastoids were completely dense. The other bones of the skull and face were normal. The spine and ribs were denser than when first observed. The dense band at the upper end of the humerus was 5 mm. thick and at the lower end 2 mm. thick. The upper two-thirds of the shaft revealed increased density. The scapulae and clavicles revealed involvement. The entire pelvis gave evidence of increased density, which was least marked in the ischium and pubis. The floor of the acetabulum was definitely involved. The dense band at the lower end of the femur was 5 mm. thick and the bands at the upper ends of the tibiae and fibulae were of the same thickness. The clubbing or lipping was clearly shown here. The head of the humerus was 15 by 7 mm. and the head of the femur was 9 by 3 mm. In the center of the head of the femur there was a dense dot which might be the beginning of the marbling process although in the other bones it had started at the periphery. At examination in 1935, some increase in the density of the sella turcica and slight increased density around the mastoid antrum were observed. The thorax, spine, pelvis and upper part of the femurs revealed uniform increase of the disease. The epiphyses of the heads of the femurs and trochanters were now normal in size. The lower half of the femur and upper 2 inches (5 cm.) of the tibia and fibula were very dense. The lower part of the forearm, wrist and hand revealed only slight involvement. The lower end of the tibia, and fibula and the bones of the feet revealed changes more marked than were noted previously, but not as much as were seen in the other cases in proportion to the involvement of the other bones. Erythrocytes numbered 4,540,000 and the concentration of hemoglobin was 85 per cent.

Case VIII. F. K., a girl, aged eleven months, was first seen in May, 1930. A roentgenogram at this time included the entire spine, pelvis, upper ends of the humeri and femurs. The only changes were a 5 mm. band of density at the upper end of the humerus and a similar band at the upper end of the femur.

Ten months later, in April, 1931, roentgenograms of the vertebrae revealed a very narrow, dense band along both the superior and inferior borders. The upper ends of the humeri gave evidence of involvement for the upper 3 cm. and the trabeculations here were practically obliterated. Similar changes had taken place in the upper ends of the femurs. The lower ends of the femurs and the upper ends of the tibiae revealed bands which were 7 mm. thick.

Re-examination in 1935 disclosed no definite evidence of the disease in the skull. The dense bands in the vertebrae had become thicker. The pelvis and upper femurs revealed an increase in density. The lower end of the femur, and the upper ends of the tibia and fibula revealed definite increase in density which was progressing as in the other cases. There was a 3 cm. band at the lower part of the diaphysis of the tibia; there was some increased density of the astragalus and less density of the other tarsals. The lower ends of the radius and ulna disclosed a narrow band of increased density. The carpals, metacarpals, and phalanges were normal.

The remaining child, D. K., a girl, aged nine, was first seen in 1929. She is not included with the foregoing cases, as no evidence of the disease was present. She was re-examined again in 1935, but still no evidence of the disease was observed. Instead, there apparently was slightly less calcium in her bones than in normal bones.

SUMMARY

Eight cases of osteopetrosis (marble bones) are reported; the condition occurred in three generations of the same family. Five of these patients were examined at various intervals during the preceding five years, and the changes found have been noted.

The disease can be transmitted by either sex and affects both sexes equally.

The disease has been divided into two types, a "malignant" type and a "benign" type, according to the course it runs; this course can be predicted roughly.

The ages of the patients varied from eleven months to seventy-two years.

There may be no symptom of the disease

or there may be a history of repeated fractures following mild trauma. The disease is always widespread throughout the skeleton, and is never confined to a single bone or to an isolated section of the body.

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MULTIPLE MYELOMA AND ASSOCIATED RENAL LESION

A REVIEW AND CASE REPORT

By M. BARFIELD-CARTER, M.D.
BIRMINGHAM, ALABAMA

MULTIPLE myeloma is a rare, highly malignant bone tumor arising from the bone marrow. It is characterized by pain, multiple destructive foci in the bones of the skeleton; anemia; and usually by the presence of Bence-Jones proteinuria and renal pathology. It occurs chiefly between the ages of forty and sixty, although a few cases have been reported in young adults and children.[3,5,10,12,21] It metastasizes rarely except to bone, and is always fatal. Jacobson,[11] in 1917, reported a case of multiple myeloma with a good description of the renal condition associated with the disease, but it has been only recently that much attention has been called to this complication. For this reason, major emphasis is placed on the kidney pathology in reporting the following case.

This pathological entity, now called multiple myeloma, was first described in 1850 by MacIntyre.[14] The case which he reported had been seen in association with Bence-Jones who examined the urine and reported an abnormal finding which he described as "animal matter"; and Dalrymple[4] who made the "microscopic examination of the two affected ribs." In 1873, Rustizky[19] recognized this condition as a specific disease of the bone marrow and suggested that it be called myeloma. Kahler[13] in 1889 associated multiple myeloma with the excretion of Bence-Jones bodies, hence the reference to "Kahler's disease" in some of the literature.

Pain is the outstanding feature of the condition. In the beginning, this pain is often vague and indefinite, being transitory in duration and location, but having a tendency to be most frequently located in the region of lumbar spine. Pathological fractures are frequent, particularly in the ribs. Often the first indication of the disease is a fracture following slight trauma or sudden motion. Neurological symptoms are not uncommon.

Roentgenologically, the individual lesions of multiple myeloma appear as small, round, punched out areas varying in size from 1 mm. to 1 cm. in diameter, the most typical appearance being found in the skull in which there are usually multitudinous lesions. These lesions are entirely osteolytic with no attempt at new bone formation and appear in the skull, vertebrae, ribs, sternum, clavicles, and later in long bones. This condition must be differentiated in the roentgenogram from hyperparathyroidism, and hypernephroma and carcinoma which have metastasized to the bones.

The multiplicity of the bone tumors is a striking feature. It is impossible to be certain whether the initial lesion is a local one with early multiple metastases or originates simultaneously in a number of bones. Although the multiplicity has been emphasized in the majority of cases, single lesions have been reported by Geschickter and Copeland,[10] Rogers,[18] Venable[24] (this case was single on March 7 and became multiple on April 16), Carlson[3] and Cabot.[2]

The blood picture in most of these cases is characterized by a secondary anemia which increases as the underlying pathology progresses. The flat bones are the first involved and since these are the bones containing red marrow, and since the marrow is replaced by the tumor tissue, a marked secondary anemia gradually develops. Other than a secondary anemia, there are no constant characteristic blood changes. The fact that blood smears showed a profound rouleaux formation and that precipitation occurred in the red pipette when blood was mixed with Hayem's solution was first reported by Reimann.[17] From

such a finding, he was led to suspect hyperproteinemia and as a cause for this, multiple myeloma. He also reported a rapid sedimentation rate. Cases of hyperproteinemia associated with multiple myeloma have been reported by Foord,[7] 4 cases, Perlzweig, Delrue, and Geschickter,[16] Sweigert,[22] Shirer, Duncan and Haden,[20] and Foord and Randall.[6] High protein values are not, however, specific for multiple myeloma, as they are found, though rarely, in other conditions.

The presence of Bence-Jones protein in the urine of these patients is common but not constant. Geschickter and Copeland[10] found this substance to be present in approximately 65 per cent of their cases of multiple myeloma, but by no means specific for the disease. It may be found in other conditions such as myxedema, carcinoma with metastases to the bones; osteomalacia; and leukemia, and vice versa, many cases of multiple myeloma are reported in which the Bence-Jones proteinuria is absent. The exact nature of this substance is not yet understood. In the case report given below, repeated examinations showed the urine to be negative for Bence-Jones protein, although a heavy trace of albumin was always present.

In the more recent literature, nearly all the authors who have reported cases of multiple myeloma have found associated pathological lesions in the kidneys; but they are so varied that it seems impossible to attribute any particular one to myeloma.

Bell[1] has tabulated 79 reports from the literature dealing with renal changes associated with multiple myeloma and added 11 which he reports in his own article, making 90 in all. He summarizes the structural changes in the kidneys and concludes that renal insufficiency frequently develops in advanced stages of multiple myeloma and that in some instances it is due to arteriosclerosis or pyelonephritis resulting from cord compression or prostatic hypertrophy. Also, he concludes that Bence-Jones protein forms tubular casts which obstruct the tubules and causes tubular atrophy leading to renal insufficiency; and further, he states that the renal pathology resulting from Bence-Jones protein is due to mechanical trauma and not toxic injury to the glomeruli or tubules.

Forbus, Perlzweig, and Burwell,[8] in a study of the effect of Bence-Jones excretion on the kidneys, state that the lesion is a tubular obstruction which may be compared with that which follows any form of obstruction within the urinary tract. This explanation was first suggested by Thanhauser and Krauss. In a second report, Forbus and his associates[9] studied the effect of Bence-Jones excretion on the kidneys in a patient and concluded that although they were dealing fundamentally with an obstructive lesion, there were certain peculiarities about it which differentiated it from other obstructive lesions of the kidney and set it aside as a specific one dependent on Bence-Jones protein. This peculiarity is a cellular reaction about the casts. From their experimental study on dogs, rabbits and mice, they found that the injection of Bence-Jones protein caused a shock to the animals which manifested itself by vomiting and malaise which soon disappeared. There was no injury to the kidney epithelium that could be seen microscopically, and there was no kidney functional disturbance of any significance. By producing a chronic partial urinary obstruction in one of their dogs, they were able to "facilitate the precipitation of Bence-Jones protein in the kidney tubules" but the foreign body reaction characteristic of the human kidney was not present. They concluded that the excretion of this protein produces a specific anatomical injury to the kidney if the amount of protein is large enough and is excreted over a prolonged period of time. The case reported below shows, in addition to the arteriosclerotic changes, a lesion similar to the obstructive ones described above; but the Bence-Jones protein was consistently absent in the urine throughout the entire course of the disease; however, a large amount of serum albumin was always pres-

ent in the urine. Unfortunately, there was no estimation of serum protein. The case would most probably have shown a hyperproteinemia.

Perla and Hutner[15] reported 2 cases which they called "nephrosis." In Case 2, the urine contained large amounts of serum albumin but no Bence-Jones protein. The kidneys in this case showed casts and tubular atrophy but nothing indicative of arteriosclerosis or complicating infections. The fact that the Bence-Jones protein was absent in the urine is of little significance because the case was under observation for one week only.

CASE REPORT

E. R., white male, aged fifty, entered the outpatient clinic of Hillman Hospital July, 19, 1933, complaining of pain in upper abdomen. He stated that the pain moved about, being sometimes on one side, sometimes on the other. His weight decreased from 145 to 115 pounds. Patient was admitted to the hospital for diagnosis and treatment August 17, 1933. His chief complaint was "pain in the back." Eight months prior to admission he began to develop pain in his back after any form of labor and the pain caused him to remain in bed for several days. He had his teeth extracted and the pain seemed to improve. Two weeks prior to entering the hospital, he began having pains again in the lumbar region which now radiated down the right thigh. It bothered him more when he worked and he was unable to stoop. His past history was irrelevant.

Physical examination showed a white male, aged fifty, underweight, and apparently in pain. *Skull:* normal in size and shape. *Pupils:* react to light and accommodation. *Nose:* negative. *Tonsils:* red and atrophic. *Neck:* negative except for arterial pulsation. *Thorax:* expansion equal, but restricted; pigeon breast configuration; complained of pain on pressure; breath sounds distant but no râles. *Cardiovascular system:* arrhythmia with slight enlargement to percussion; no murmurs; sounds faint; blood pressure 170/100; generalized arteriosclerosis. *Abdomen:* no palpable masses. *Spine:* there is a mass over spine of left scapula which feels like a bone. The spine is limited in motion in all directions. Skin, extremities, and reflexes normal. *Impression:* Chronic atrophic arthritis. Myocardial degeneration. Bone tumor of left scapula.

Laboratory findings were as follows: *Urine:* reaction, acid; specific gravity, 1.004; albumin, slight trace; sugar, negative; few leukocytes and uric acid crystals; Bence-Jones protein, negative. *Blood:* hemoglobin, 70 per cent; red blood cells, 3,590,000; white blood cells, 6,150; differential count: lymphocytes, 38 per cent; large monuclears, 2 per cent; neutrophiles, 59 per cent; eosinophiles, 1 per cent. No estimation of serum protein. *Gastric contents:* total acidity, 60 per cent; free HCl 40 per cent; lactic acid positive and occult blood negative.

Roentgen Examination. The spine showed a marked decalcification of all vertebrae with numerous small punched out areas of destruction. In addition, there was a degenerative arthritis with spur formation of all lumbar vertebrae. The same destructive process was noted in skull, ribs, upper third of humeri, tibiae, fibulae, and femora.

His temperature varied from 97 to 99°. He was given palliative treatment, a body cast applied, and discharged on September 1, 1933. He was readmitted October 29, 1933, with greater pain in back, legs, and chest. One week before readmission he had sharp, severe pains in chest on pressure or motion such as breathing or coughing, and it was because of this extreme pain that he returned to the hospital. He showed marked emaciation, deformity of anterior chest wall, and peculiar crackling sensations in ribs. At this time numerous examinations of the urine showed specific gravity varying from 1.010 to 1.017; albumin 250 to 1,000 mg. per 100 c.c.; Bence-Jones protein negative; many hyaline and waxy casts, mucus and epithelial cells. The blood examination was as follows: hemoglobin, 64 per cent; red blood cells, 3, 420,000; white blood cells, 9,400 with 22 per cent lymphocytes and 78 per cent neutrophiles; calcium varied from 11.9 to 17.4 mg. per 100 c.c.; phosphorus 3 to 4.4 mg. per 100 c.c. Roentgen examination showed the same areas of destruction in skull, ribs, humeri, femora, tibiae, fibulae, and spine but to a more marked degree. Hypertension, arteriosclerosis, and nephritis were present. Patient died on December 15, 1933, of a hypostatic pneumonia.

ABSTRACT OF AUTOPSY REPORT

External Examination. The chest is elongated and irregularly flattened showing a peculiar deformity. There is a prominence of the precordial chest plate

with depression of the manubrium and marked bilateral depression in both mammary areas. The outer ends of costal cartilages are thickened and there is a sharp depression where the ribs join them. The ribs are flexible and when pressed upon there is a crackling sensation elicited suggesting fractures. No external deformity of cranial or facial bones.

Thoracic Cage. There is a well-marked deformity of the ribs with numerous old and fresh fractures; deformities due to thickenings that appear to be callus formation and numerous fractures without blood extravasation.

Vertebrae. On pressure, the vertebrae give the same crackling sensation as was noted in the ribs and the saw cuts through them readily. The cortical shell is thin and paper like and there seems to be little or no centrum, the space being filled by red marrow. Spontaneous fracture of first lumbar.

Neck. There is a small adenoma, 0.7 cm. in diameter, at the junction of isthmus and right lobe of thyroid. There is a definite 6 or 7 mm. mass appearing like parathyroid at lower margin of right lobe. A similar mass projects below left which appears to be continuous with left lobe. These are the only bodies found likely to prove parathyroid. A few lymph nodes are noted overlying the trachea. No thymus tissue.

Peritoneal Cavity. Negative.

Heart. Negative.

Lungs. Pleural cavity negative. Little old scarring at left apex and a few shotty nodules scattered over surface beneath the pleura. Moderate hypostasis and slight pneumonic infiltration. Middle lobe shows an area of increased density overlaid by a fibrous deposit. Lower lobe on right shows well-marked congestion and numerous pus droplets in bronchial lumen.

Fig. 1. Roentgenogram of the skull showing multiple destructive areas.

Fig. 2. Roentgenogram showing multiple destructive areas in spine and pelvic bones.

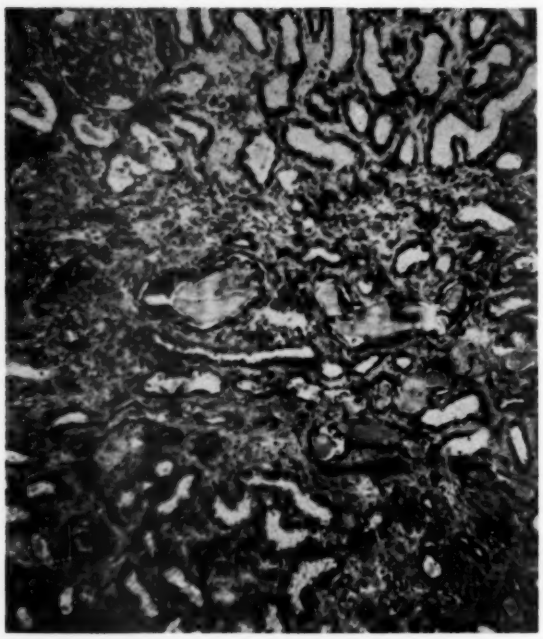
Liver. Essentially negative.

Spleen. Weighs 163 gm. On convex surface there is a small firm nodule 3 cm. in diameter and a calcified lymph node at hilus. Malphigian corpuscles are dull whitish gray and translucent. Occasionally, there is scattered through the parenchyma, small yellow white nodules about 1 mm. in diameter which contain a firm caseous material.

Kidneys. Weigh 267 gm. Left: The surface is somewhat discolored, a light yellow. Capsule strips easily leaving a smooth surface. Few small scars of surface and one small yellow spot about 2 mm. in diameter. Cortex is 5 mm. thick, pale yellowish white in color with an occasional streak of red perpendicular to surface. Pelvic mucosa reddened. Right: Surface has a number of scars and a few small cystic areas. Surface vessels engorged. Tissue is more vascular than left. Other findings same as left. Adrenals are bright yellow in color and medulla rather thick and grayish white.

Gastrointestinal Tract. Negative.

Head. Scalp negative. Calvarium cuts with more ease than usual and is rather thin, varies from 3 to 6 mm. in thickness. The diploe is poorly marked but in the lower parietal, on the right side, there are several dull red patches visable on inner table and here there is a lake-like formation of marrow. Sinuses negative. Brain shows no gross lesions. Lateral ventricles negative.



A

B

FIG. 3. Section of kidney showing large casts obstructing tubules and foreign body cell reaction. *A*. Low power. *B*. High power.

Femur. The shaft in upper midportion was opened. Cortex of natural density but the marrow cavity shows irregular enlargement. It is stuffed with a dull red to yellowish gray marrow of natural consistency.

Anatomical Diagnosis: Multiple myeloma; chronic nephritis; hypostatic pneumonia.

The microscopic examination of tissue from ribs and femur showed multiple myeloma, plasma cell type. A detailed report by Dr. G. S. Graham of microscopic examination of the kidney lesion is as follows: "There is a well-marked fibrosis both as a slightly developed generalized lesion and as frequent small radial wedges in which the glomeruli are sclerotic, the tubules atrophied and the stroma infiltrated by lymphocytes. There is arterial and arteriolar sclerosis especially marked in the smaller vessels. The tubular epithelium is variable in its appearance. In the convoluted tubules the cells are sometimes low or cuboidal and again swollen and filled with fine or coarse hyaline droplets. Large numbers of casts are present in both cortex and medulla. They are sometimes of the usual hyaline type but in most cases their substance appears denser, variable in staining reaction and very commonly resistant to all stain. The outlines are often irregular or there is an appearance of fracturing and again of lamellation. Marked cellular disturbances are associated. The cells occur within but especially about the casts. These are sometimes leukocytes and again they are epithelial. Multicellular masses of giant cell type are sometimes applied to the cast surface. The lining epithelium of the tubular wall is variously distorted and one gets the suggestion that it is suffering injury, mechanical or chemical, by the cast material while the injured cells are being irregularly replaced by regeneration. Very rarely there is a mitotic figure to support the suggestion. There is slight generalized increase of the stroma in the medulla. The cellular disturbances within the cast-bearing tubules are the same here as in the cortex.

"*Comment*: A part of the changes present are to be credited to the existence of a low grade vascular nephritis. On top of this, there is an acute tubular irritative and degenerative lesion associated with the presence of tubular casts of peculiar type. The cast material appears to be of denser structure than the common hyaline cast and it is exciting a cellular reaction on the part of the tissues that strongly resembles that seen about foreign materials of various kinds. One is reminded especially of the reaction sometimes seen in the thyroid gland about abnormal colloid material that is being attacked by phagocytic cells within the acinar lumina."

SUMMARY

A case of multiple myeloma, which shows the typical roentgen findings and multiple pathological fractures, has been reported. Generalized arteriosclerosis and a chronic nephritis were present as complications.

The pathological report of the kidney showed an arteriosclerotic form of nephritis complicated by an acute tubular irritative and degenerative lesion associated with the presence of peculiar tubular casts. This picture is similar to the findings reported by Forbus and others as being an obstructive reaction due to the presence of Bence-Jones protein, although this protein was consistently absent in the urine throughout the course of the disease. Unfortunately the protein estimation of the blood was not made.

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BENIGN ADENOMA OF THE BRONCHUS

By HAROLD O. PETERSON, M.D.

Department of Roentgenology, Massachusetts General Hospital
BOSTON, MASSACHUSETTS

BENIGN adenomata constitute approximately one-half of all the benign bronchial tumors ever reported. The first case was discovered at autopsy by Mueller in 1882, and since then approximately 43 cases have been reported which can be classified in this group. Because these tumors are not generally recognized, even by pathologists, many of the reported cases as well as 4 of the 9 forming the basis of this paper were originally mistaken for bronchogenic carcinoma.[5,8,10,11,13,15,20] A few have undoubtedly been considered as cures of carcinoma of the lung following radical surgery or even simple bronchoscopic removal. With early treatment the prognosis is excellent but if allowed to continue untreated the majority develop atelectasis and extensive pulmonary suppuration which eventually causes death. For this reason the prompt and correct diagnosis is of considerable importance.

A detailed description and illustration of the roentgen findings will be presented in this paper. The entire literature has been reviewed and any statistics stated are based on the 43 cases found there plus the 9 which we have studied. A short description of the clinical and pathological findings will be given, however, because of their significance in interpreting the roentgen picture. The case reports and the clinical, surgical and pathological aspects of benign bronchial adenomas will be discussed more completely in a forthcoming paper from the Thoracic Service of the Massachusetts General Hospital.

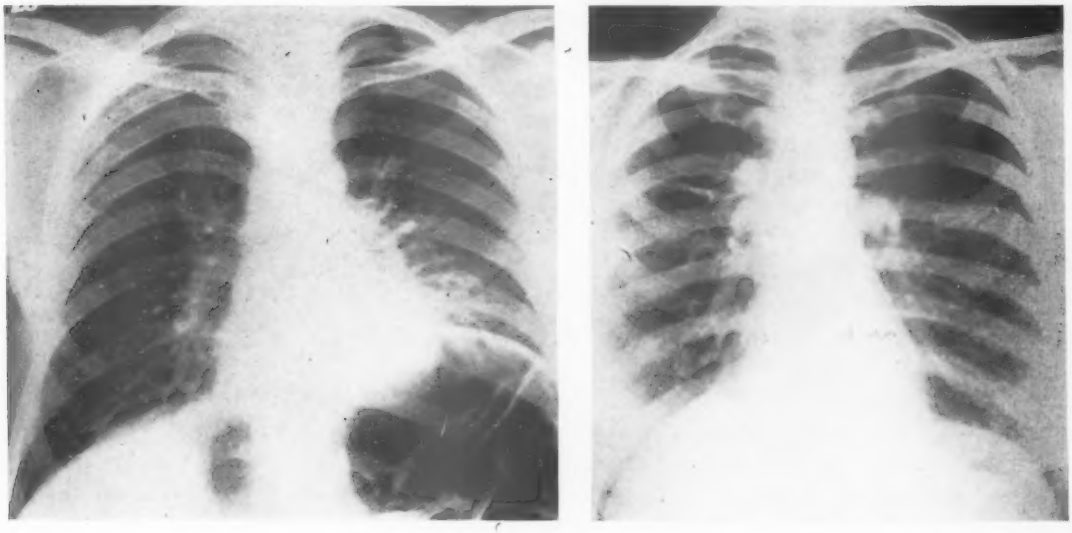
A history of repeated hemoptysis over a period of months and years should at once suggest the possibility of a benign bronchial adenoma. The hemoptysis, which is described by many authors as beginning and ceasing abruptly, occurs in the majority of the cases, is usually repeated, may be the first complaint and may continue as the only complaint. Two cases have been reported in which repeated hemoptysis was the only symptom for twenty and thirty years respectively.[13,20] A dry non-characteristic cough, which frequently becomes productive, is almost always present. Pain and soreness in the chest is emphasized by some authors,[5,18,19] and was found in 8 of our 9 cases. Pleurisy and repeated bouts of pneumonia are common complications. Dyspnea is not a prominent symptom but severe attacks on lying down have been reported, presumably due to a pedunculated tumor rising suddenly into the trachea.[20]

The age incidence varies from eleven to sixty-seven years but 50 per cent occur between the ages of twenty and forty. In contrast to carcinoma of the lung, benign adenomas are found less often in males than in females; i.e., 21 males and 31 females.

The physical findings are those produced by a partial or complete bronchial obstruction and may vary from nothing at all to signs of complete atelectasis of an entire lung. As the disease progresses all the signs of chronic pulmonary suppuration may develop.

For a description of the bronchoscopic findings, the reader is referred to the numerous papers already published by the bronchoscopists who are largely responsible for the rediscovery and recognition of this tumor.[7,8,9,13,15,19]

The treatment of these cases is also in great part a bronchoscopic procedure. The tumor can be removed through the bronchoscope if it does not extend outside the wall of the bronchus. Such methods as diathermy, piecemeal removal with biting forceps and the placing of radon seeds in the base are used.[7,8,9,13,15,19] Repeated bronchcoscopies are usually required to completely destroy the tumor. When bron-



a *b*

FIG. 1*a*. Case I. The tumor was found by bronchoscopy partially obstructing the left lower lobe bronchus ¼ inch below the opening of the upper lobe bronchus. The atelectasis shown in the above film disappeared after removal of the tumor but the high left diaphragm persisted.

FIG. 1*b*. Case II. Tumor 0.9 by 0.7 by 0.6 cm. found on bronchoscopy, and later confirmed by autopsy, partially occluding right upper lobe bronchus. The narrow band of atelectatic lung tissue seen in the first right interspace was the only roentgenographic evidence of the tumor's presence.

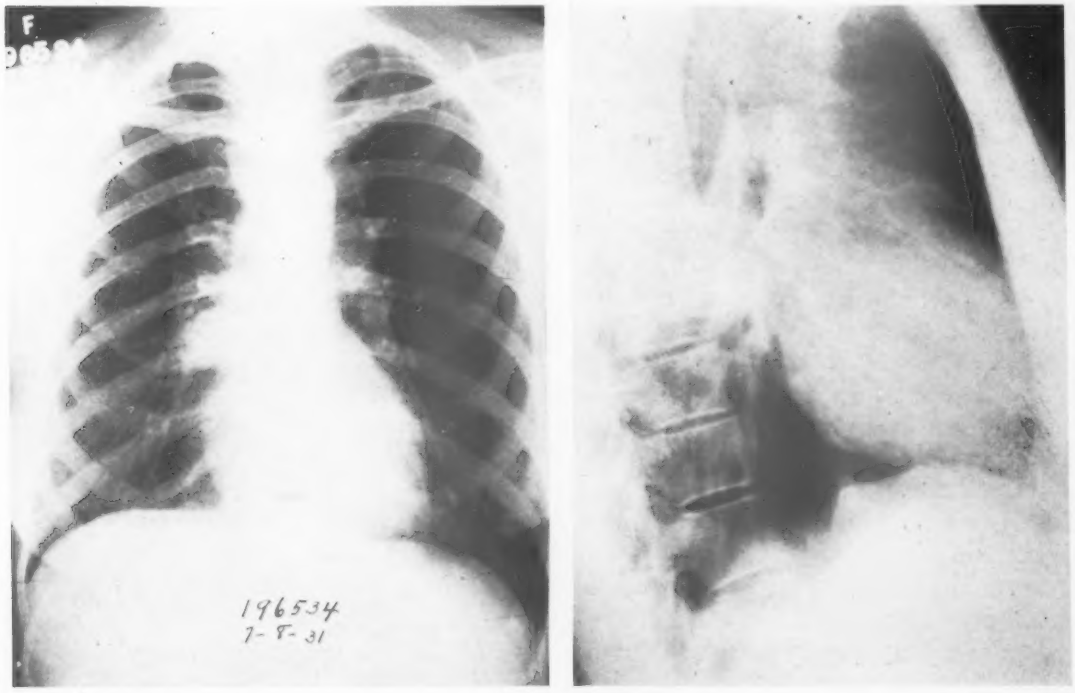


FIG. 2. Case III. Pedunculated tumor completely intrabronchial partially obstructing bronchus to right lower and middle lobes was found on bronchoscopy and confirmed by operation. The mass seen in the right hilus is produced by the tumor together with an area of atelectasis and suppuration in the upper medial part of the lower lobe (see also Fig. 9*a*).

chiectasis and pulmonary destruction are present, or if the tumor extends outside the bronchial wall, radical surgery such as lobectomy or pneumonectomy is indicated.[8, 9] Deep roentgen therapy is of doubtful value, although cessation of hemoptysis has been reported following its use.[20]

Grossly the tumor is attached to the wall of a larger bronchus usually by a broad pedicle. Although the majority are entirely endobronchial, occasionally the tumor extends through the wall and a second mass develops outside the bronchus. The size of the tumors varies from a few millimeters to that of grapefruit, as was seen in a case reported by Kramer and Som.[9] The surface of the tumor is smooth and often lobulated. It does not infiltrate the lung parenchyma locally or metastasize elsewhere. The lung beyond the tumor shows varying amounts of atelectasis, bronchiectasis, parenchymal suppuration and cornification. Empyema is a frequent complication of those cases which have extensive pulmonary infection. Two patients reported by Geipel[5] died from uremia and at autopsy showed extensive generalized amyloidosis due to the long standing pulmonary suppuration.

Microscopically the tumor has often been incorrectly diagnosed as a carcinoma, probably because a benign bronchial adenoma was not known to exist. The exact origin of the neoplasm is still not definitely established, but it probably arises either from the mucous glands or their excretory ducts.[17] The histologic picture is one of anastomosing columns of cuboidal cells with a tendency to glandular formation and an absence of mitosis. The stroma is often richly vascular which probably accounts for the tendency to hemorrhage.

The roentgenological findings are almost solely those of bronchial occlusion of varying degree depending on the size, location and length of time that the tumor has been present. The tumor itself is rarely seen because it is so small and usually is obscured by the collapse it has produced. It is conceivable that the tumor might be so small it would not even interfere with the aeration of the lung. In that event the roentgen examination would be completely negative and such a case has been reported.[19] Fortunately the roentgenograms of all our cases have shown definite pathology. In addition to roentgenoscopy and the usual posteroanterior films of the chest, the straight lateral view as stressed by Hampton and King[6] has become indispensable for correct diagnosis and accurate localization.

Because these tumors grow so slowly there is a long period during which the bronchus is only partially obstructed. One would expect the dependent lung to show either atelectasis or an obstructive emphysema. All our patients developed atelectasis and in no instance was there any evidence of an obstructive emphysema. The atelectasis can be divided very conveniently into three general types depending on the degree and location of the obstruction.

The first type occurs when there is partial obstruction of any large bronchus. The involved lung becomes less radiant than normal and usually shows linear areas of increased density produced by the bands of atelectatic lung tissue (Figs. 1 and 2). The diaphragm is frequently elevated, moves poorly on respiration and the mediastinum moves toward the involved side on inspiration. This motion of the mediastinum as seen during roentgenoscopy or on films made at inspiration and expiration is of great diagnostic significance for any type of bronchial obstruction and may be the first clue towards the correct diagnosis.

In the second type there is complete obstruction of a secondary bronchus causing total atelectasis of the dependent lung. The collapsed portion can now be seen as a triangular dense area usually along the diaphragm, heart and spine (Figs. 3, 4 and 5). It is possible for the shadow of the collapsed lobe or lobes to be almost completely hidden within the heart shadow and even overlooked on casual examination (Fig. 3). The diaphragm may be in normal position and move fairly well on respiration. The

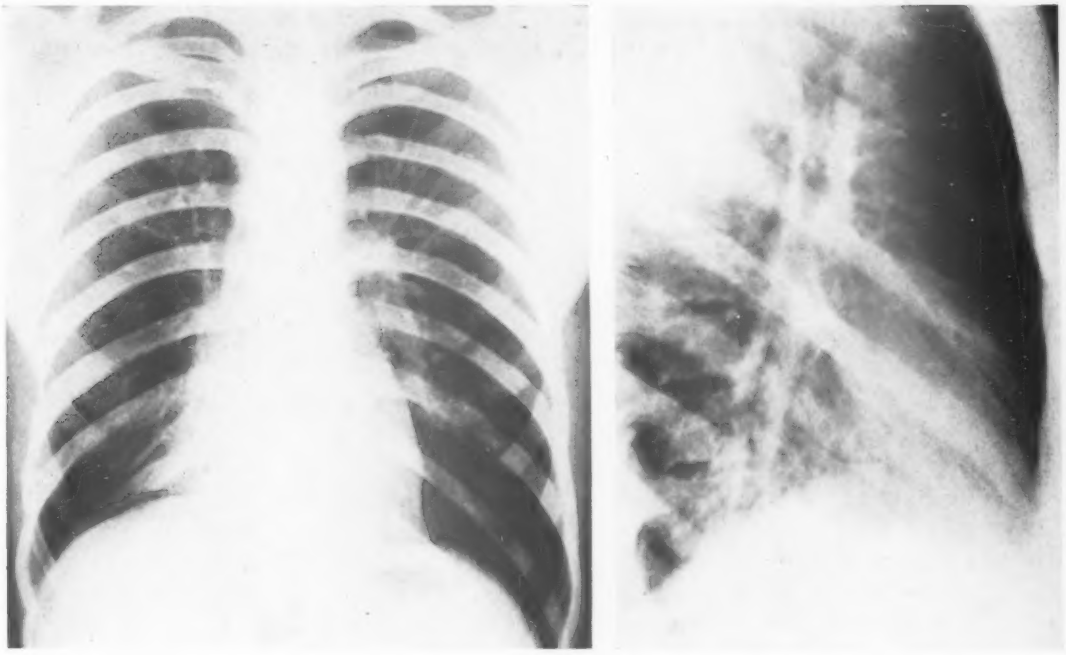


Fig. 3. Case IV. Tumor 1.5 by 1.0 by 0.7 cm. completely filling lumen of bronchus to right middle and lower lobes was found on bronchoscopy, and an adjoining tumor mass 1.3 cm. in diameter outside the bronchus was later discovered at operation. Note the absence of the right hilus, decrease in the vascular markings throughout the right lung field and the increased density obscuring the right heart border. The emphysematous upper lobe fills the entire right half of the chest. The lower and middle lobes are completely collapsed and can be seen in the lateral view as dense bands running from the hilus to the diaphragm (see also Fig. 9*b*).

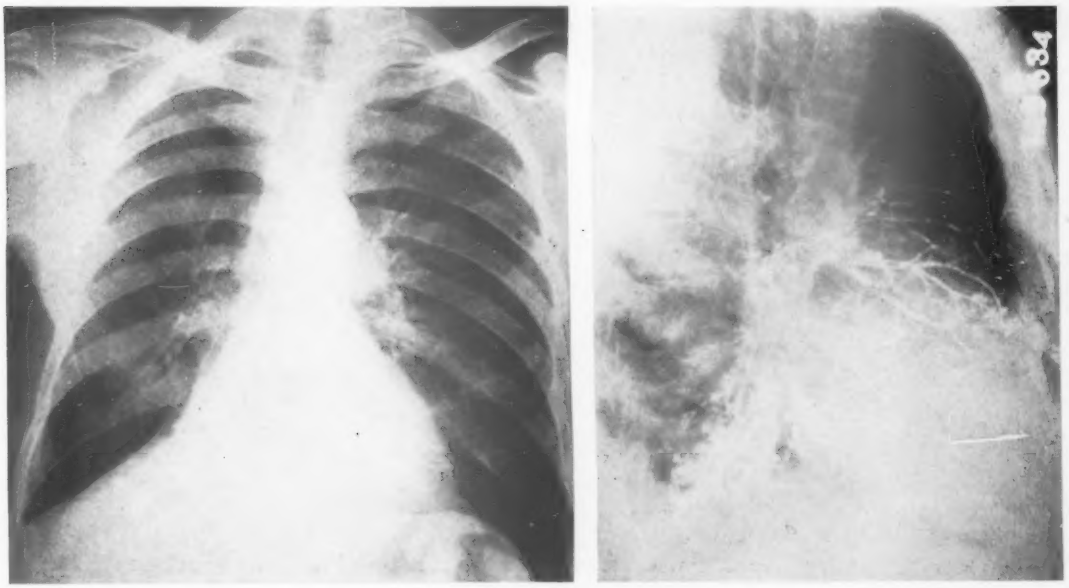


Fig. 4. Case V. Mass was found on bronchoscopy completely occluding lumen to right middle and lower lobes. The roentgen findings are essentially the same as in Figure 3. In addition to obscuring the right heart border the collapsed lower and middle lobes also obscure the diaphragm. The lateral view was taken after the tumor had been removed and lipiodol injected and it shows a moderate degree of bronchiectasis (see also Fig. 9*c*).

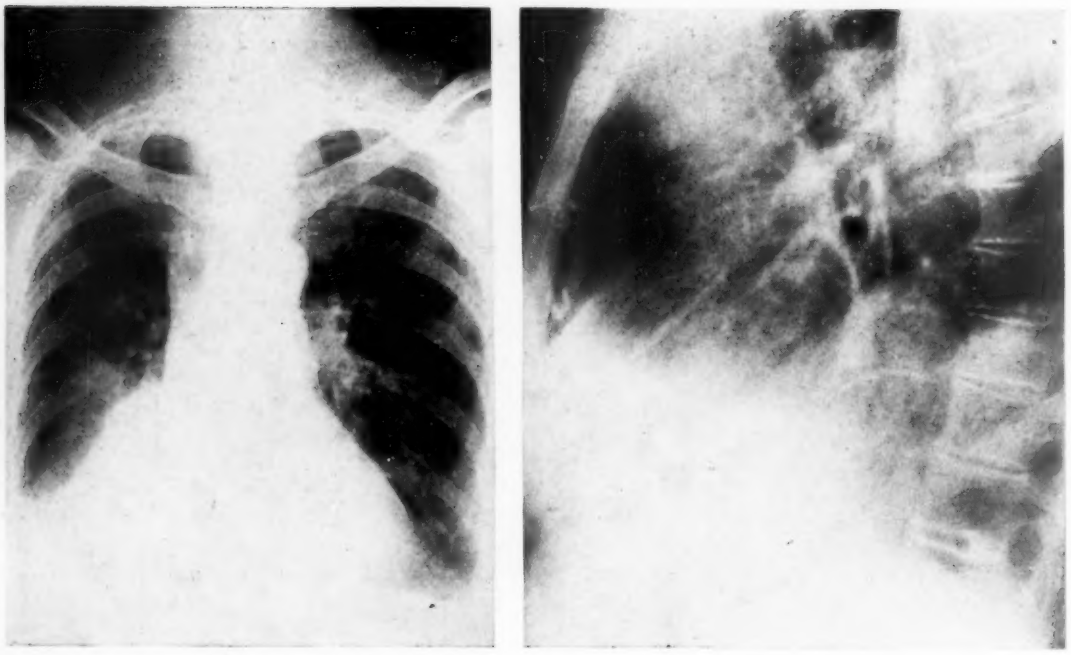
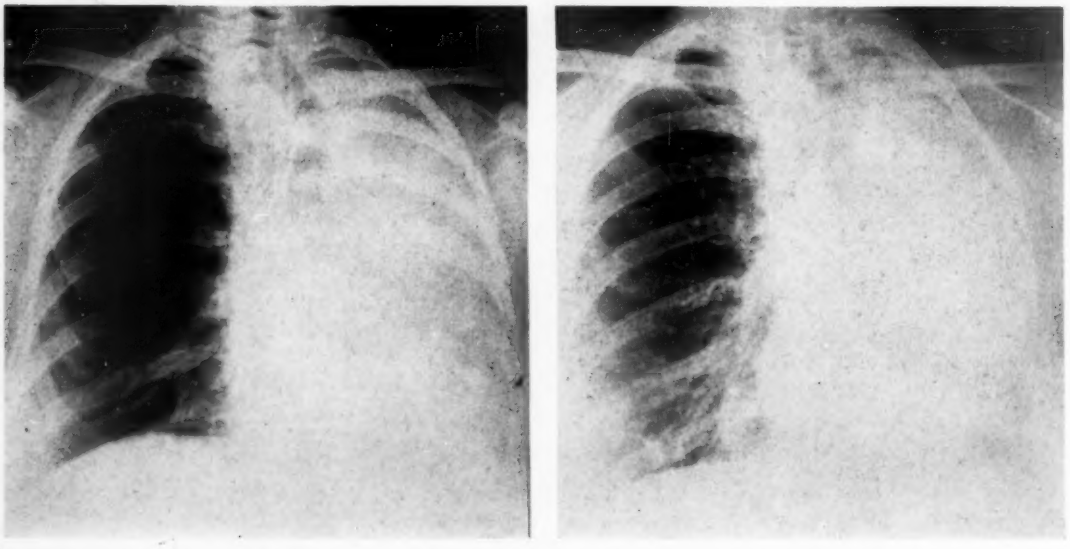


Fig. 5. Case vi. Tumor found at the first bifurcation of the right lower lobe bronchus at autopsy. Shift of the mediastinum to the right on inspiration was noted during roentgenoscopy. Note the dense area obscuring the right heart border in the posteroanterior view and the right diaphragm in both views.



a *b*

Fig. 6*a*. Case vii. Tumor 1.5 by 1.9 cm. was found on bronchoscopy and later by operation to be completely obstructing the left main bronchus. There is a marked permanent displacement of the trachea and mediastinum into the left lung field and homogeneous density throughout it.

Fig. 6*b*. Same patient five months after total left pneumonectomy. The slight return of the heart towards the right side is due to postoperative pleural effusion which was much more extensive shortly after the operation.

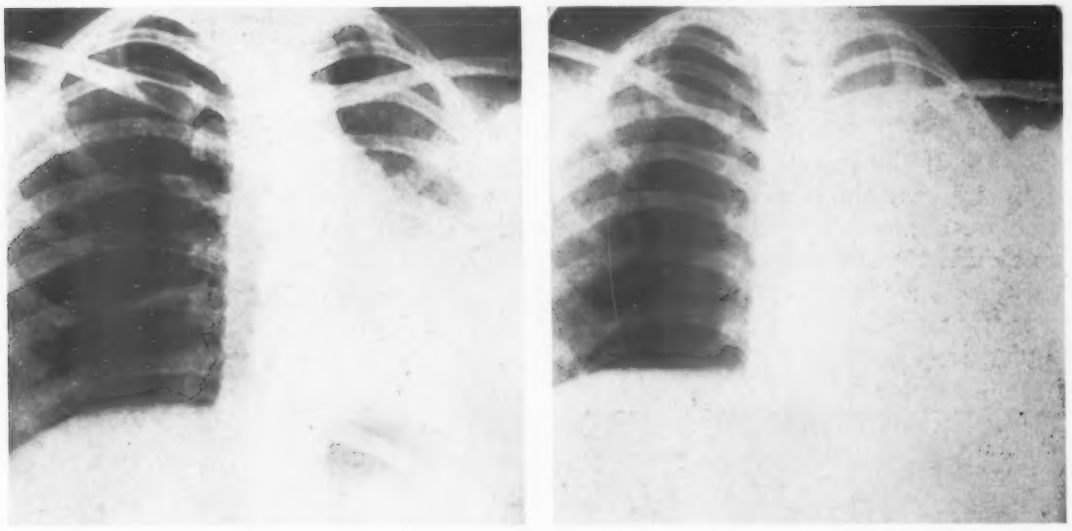
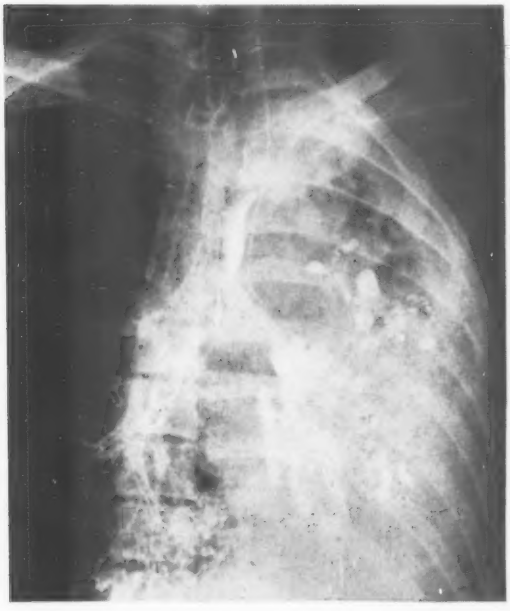


Fig. 7. Case VIII. Tumor 2 by 1.5 cm. completely occluding left main bronchus was found by bronchoscopy and later at autopsy. The films show partial and later total collapse of the entire left lung.



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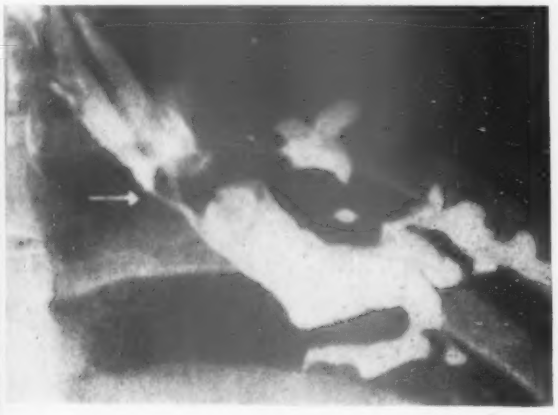


b

Fig. 8*b*. Same case as Figure 8*a* after injection of lipiodol through a catheter placed in a sinus tract which communicated with the bronchus. Note the filling defect produced in the lipiodol column by the tumor itself in the left main bronchus.

Fig. 8*a*. Case IX. Tumor completely obstructing left main bronchus found by bronchoscopy. Over-exposed film taken after bronchoscopic removal of part of the tumor followed by lipiodol injection. Note the large bronchiectatic cavities filled with lipiodol and air.

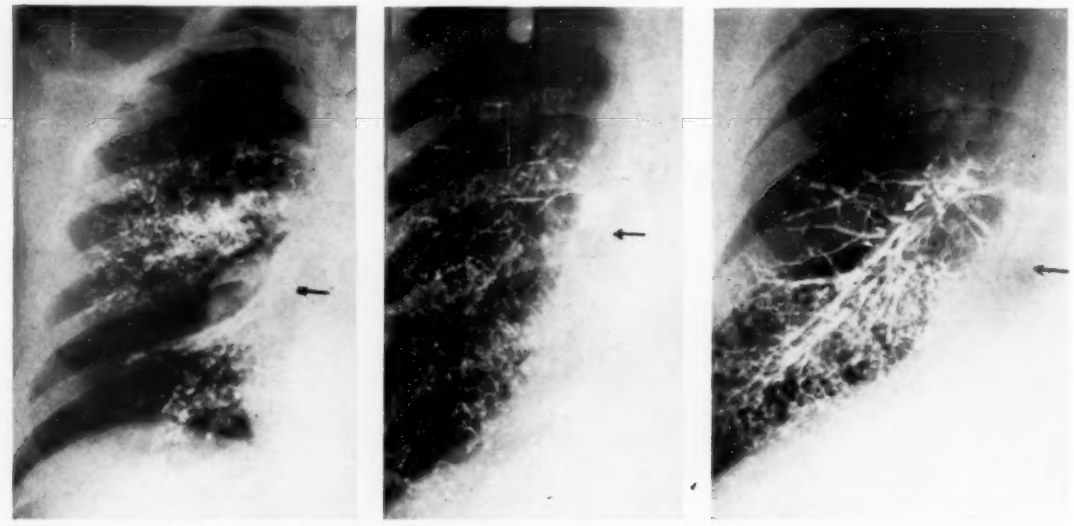
mediastinum may also be in normal position and show no shift during respiration. The involved lung field may be of normal size but will show increased radiance and a decrease in the number of vascular markings as compared with the opposite side. The hilus shadow becomes reduced in size and appears fanned out. These findings are due to the compensatory emphysema which takes place in the remaining lobe or lobes, so that by hyperexpanding they eventually fill the space previously occupied by the

whole normally expanded lung. Only long-standing bronchial occlusion, such as is seen in benign tumors, will permit all these changes to take place. The elevation of the diaphragm, shift of the mediastinum and narrowing of the intercostal spaces which one usually associates with collapse need not be present.

The third type of atelectasis occurs only when the tumor is situated in the right or left main bronchus and has completely occluded it (Figs. 6, 7 and 8). The entire

monary destruction and collapse already present, and because they are small they do not appreciably displace the mediastinum back towards the normal size.

Lipiodol has been used in a few cases and was found to be an excellent method for demonstrating the level and extent of the bronchial occlusion, as well as the condition of the lung beyond the tumor. In one patient the adenoma itself was demonstrated by injecting the lipiodol into a sinus tract which connected with the



a *b* *c*

FIG. 9. Lipiodol injection of Cases III, IV and V showing block. *a*. Same case as Figure 2. Note "cap formation" produced by the tumor in the right lower lobe bronchus and also the lipiodol coating of the right middle lobe bronchus; *b*, same case as Figure 3; "cap formation" just above the right middle lobe bronchus; *c*, same case as Figure 4. "Cap formation" difficult to reproduce because of the light quality of the film. The filled bronchi are all part of the upper lobe.

half of the chest is extremely dense, obscuring the outlines of the heart and ribs; the mediastinum is permanently displaced into the involved lung field; the intercostal spaces are narrowed; and the diaphragm, which is elevated may even show paradoxical motion. Sometimes small fluid levels with air bubbles can be seen within the homogeneous density indicating the presence of pus and secretions in the dilated bronchi or parenchymal abscesses. Empyema cavities occur most commonly in this type of case but it is usually impossible to distinguish them from the extensive pul-

bronchus containing the tumor (Fig. 8*b*). The lipiodol column usually ends in the characteristic "cap formation" which may even show the lobulations of the tumor (Fig. 9*a*, *b* and *c*). We have not had sufficient experience with lipiodol injection in these cases, however, to state whether it can be used to differentiate a carcinoma from a benign adenoma. Beutel[3] in 1933 stated that there had been only 2 reported cases in which lipiodol had been used and a block demonstrated and in them the polypoid nature of the tumor had not been recognized. He was the first to make this observation

but did not feel he could diagnose a benign tumor by roentgen examination alone.

A thorough examination of the chest, which includes roentgenoscopy plus posteroanterior and lateral roentgenograms, if done with a knowledge of the clinical history, should suggest the possibility of a benign bronchial adenoma, or at least afford sufficient evidence to warrant bronchoscopy. Lipiodol injection will give added information by accurately locating the tumor and demonstrating the condition of the lung beyond it. The final diagnosis can only be made by microscopic examination of the tumor itself.

CONCLUSIONS

1. Benign adenomata make up approximately one-half of all the benign bronchial tumors.

2. The history is fairly characteristic because of the long duration and the repeated hemoptysis.

3. The roentgen findings are largely those of atelectasis of varying degrees.

4. Bronchoscopy and biopsy are necessary to definitely establish the diagnosis.

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RECURRENT IDIOPATHIC SPONTANEOUS PNEUMOTHORAX

By LESLIE K. SYCAMORE, M.D.
HANOVER, NEW HAMPSHIRE

IDIOPATHIC spontaneous pneumothorax is a condition which has aroused considerable interest in recent years. It was recognized by McDowell and by Brunniche as early as 1856, and contributions to the subject were made by Hall[5] in 1887, Galliard[4] in 1888, and Zahn[23] in 1891. It was at first considered to be a rare condition, but, as is so often the case, once the clinical entity was recognized and interest aroused, it was proved to be much more frequent in occurrence than was previously supposed. Biesenthal and Snyder[2] in 1932 found 200 cases reported in the literature up to that time, and added 12 of their own. Kjaergaard[9] in the same year mentions 200 cases in the literature and gives a careful summary of 51 cases of his own collected over a period of twenty years. In his monograph he gives an excellent discussion of the entire subject of spontaneous pneumothorax in the apparently healthy. Olbrechts[17] found 2 cases in 2,200 hospital patients suffering from pulmonary disease, and 9 cases among an unselected series of 5,500 outpatients. Wood[22] in 1931 reported 71 cases from the Mayo Clinic. In the past ten years, numerous contributions to the literature have been made. Therefore, this condition, although it must still be considered uncommon, is by no means rare.

Various causes of idiopathic spontaneous pneumothorax have been advanced. In his early contribution to the subject, Zahn[23] gives four possible etiological factors: (1) rupture of an emphysematous vesicle; (2) rupture of a pleural emphysematous bleb; (3) a tear of the lung by traction from an adhesion; (4) atrophy of the visceral pleura. Kjaergaard has established from autopsy material that idiopathic spontaneous pneumothorax may occur from rupture of air vesicles arising either from scar tissue contraction or from localized emphysematous changes without any scar tissue formation in their vicinity.

Some writers[3,18,21] have considered this condition an invariable indication of tuberculosis, either healed or active, holding that the rupture of the lung is due to a superficial focus too small for clinical or roentgenographic demonstration, or that a small subpleural focus may rupture and then undergo healing because of the collapse. Since in autopsy material scar tissue vesicles have been found most frequently at the apices, it is probable that many cases of idiopathic spontaneous pneumothorax arise from rupture of a vesicle developing in the scar of a healed tuberculous focus. In the academic sense, therefore, they may be of tuberculous origin, but from a practical viewpoint they are non-tuberculous. Kjaergaard's careful follow-up of his cases has established this condition as entirely distinct from any form of clinical tuberculosis. In this connection, however, it is well to remember that spontaneous pneumothorax is at times the initial symptom of pulmonary tuberculosis,[18] and no case should be dismissed without a careful check-up of the lung after re-expansion.

Congenital cysts have been demonstrated to be a cause of idiopathic spontaneous pneumothorax.[14,16,19,22] In some cases it may be difficult to differentiate between a congenital cyst and an emphysematous bleb, and undoubtedly some confusion has arisen in this respect. Several cases have been reported, however, in which the congenital cystic nature of the lesion has been proved.

Along more speculative lines, the theory has been advanced of a congenital weakness of the lung tissue, making it susceptible to emphysematous vesicle formation,[9,17] the occurrence of 2 cases in the same family[1,9] lending support to this con-

tention. Schomer and Ehrlich[20] postulate a failure of regeneration of the visceral pleura in replacing the superficial cells rubbed off by contact with the parietal pleura during respiration.

In the diagnosis of idiopathic spontaneous pneumothorax, certain pitfalls should be borne in mind. Clinically, pleurisy, lumbago, and arthritis may be diagnosed.[9,11,15] Occasionally the symptoms of the pneumothorax may simulate an acute upper abdominal emergency,[9,11] even leading to operation.[15] Roentgenographically, the diagnosis has been mistakenly made in cases of congenital cystic disease,[7] of a large emphysematous bulla,[8] and of an extensive tuberculous cavitation.[8] Hedblom, in discussing LeWald's case,[10] mentions the possibility of congenital absence of the lung.

Recurrence is common in cases of idiopathic spontaneous pneumothorax. It may be relapsing (on the same side), alternating (on alternate sides in successive attacks), or bilateral (on both sides at the same time). Figures on the percentage of cases showing recurrences vary from 10 per cent[12] or 20 per cent[9] to 45 per cent.[22] The number of recurrences is usually one or two, but many more may be met with. As many as eighteen attacks have been recorded.[13] The interval between attacks is usually a few months, but may be as long as twenty-three years.[1] Of peculiar interest is Hirschboeck's case,[6] with seven recurrences in twenty-one months, each coincident with the onset of menstruation.

Tension pneumothorax is a grave form of spontaneous pneumothorax. Kjaergaard had 10 such cases in his series. Prompt decompression is indicated as a life-saving measure.

The case here reported is of the relapsing type, and in one attack showed a pronounced tension pneumothorax. It is of particular interest because the emphysematous bulla which was apparently the etiological factor was plainly visible on the roentgenogram. In only one of Kjaergaard's cases was the lesion demonstrable roentgenographically, and he makes the statement regarding it that "this roentgenographic finding is quite unique."

CASE HISTORY

R. S., white male, meat cutter, aged thirty, was first seen March 30, 1936. Two years previously he had experienced a sudden onset of pain in both sides of the chest, and dyspnea.

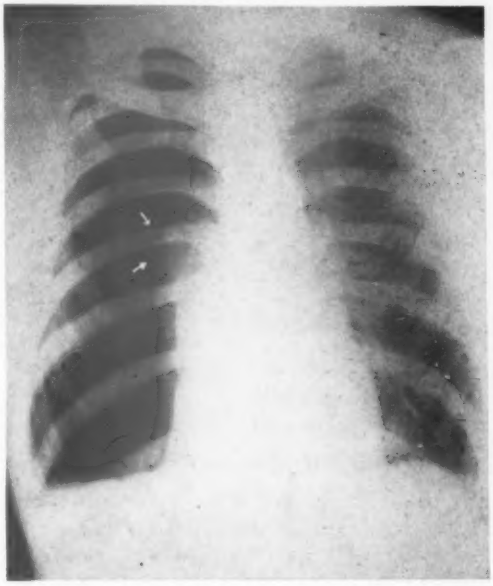

FIG. 1. Complete right pneumothorax. Note the emphysematous bleb projecting beyond the border of the collapsed lung (arrow).

A physician who was consulted diagnosed the condition as asthma. No roentgenograms were taken. The patient gradually improved and was able to return to work in about two months. A burning, cramping sensation in the right side of the chest persisted for some time. About one year later, he again had a sudden attack of dyspnea and pain, similar to the first. A roentgenogram of the chest at this time revealed the condition shown in Figure 1. The symptoms improved rapidly and the patient returned to work in a week. Three weeks later he had a third attack, and for some time subsequent to this, his physician withdrew air at intervals from his right chest. Figure 2 shows the condition present four weeks after this third attack. His symptoms gradually disappeared and he remained well until the middle of March, 1936, when he suffered a fourth attack of right-sided chest pain and severe dyspnea. He was in

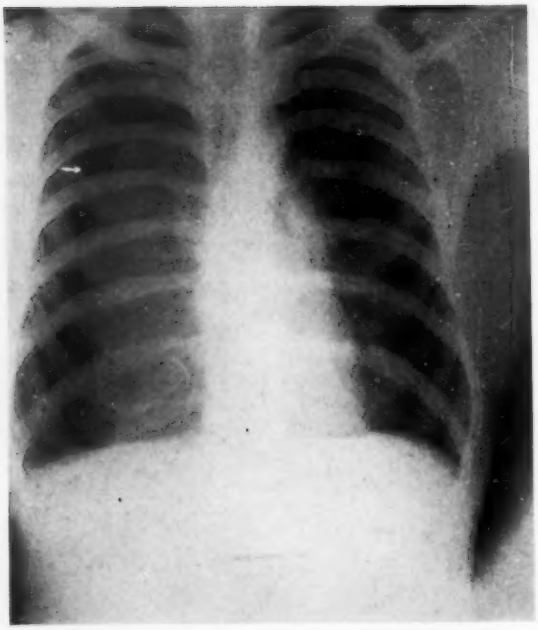

FIG. 2. Partial re-expansion of right lung. The bleb is again visible.

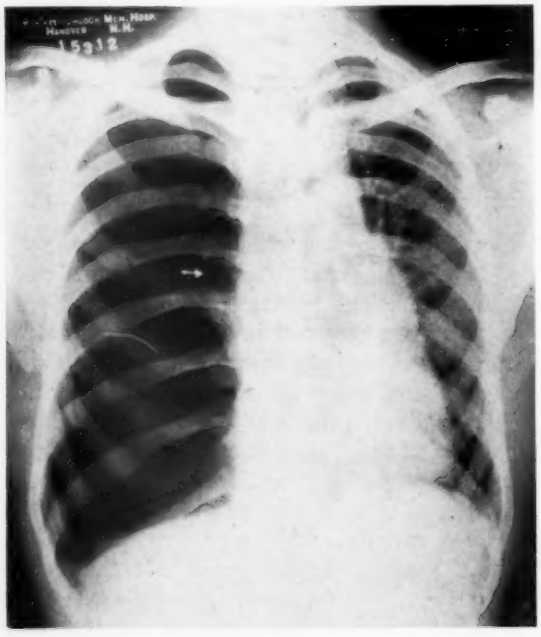

FIG. 3. Right tension pneumothorax, with marked displacement of the mediastinum. The bleb shows just to the right of the spine, and from a point immediately below it, an adhesive band extends across to the chest wall.

bed for two weeks, with only partial relief of the symptoms. At this point he was referred to the Hitchcock Clinic, and from there was admitted to the Mary Hitchcock Memorial Hospital March 30, 1936.

On admission, the patient presented a picture of extreme dyspnea and cyanosis, with shallow, rapid respiration and weak, thready pulse. The temperature was normal. Physical examination revealed the signs of a right pneumothorax. Roentgenogram showed a right tension pneumothorax (Fig. 3). The patient's acute symptoms were relieved by aspiration of air

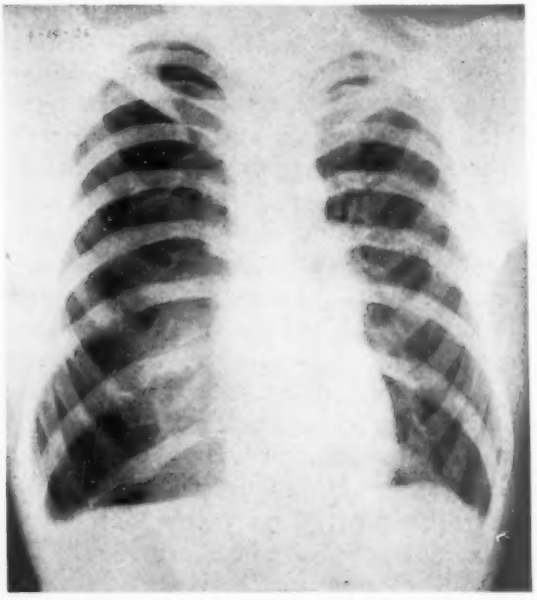

FIG. 4. Partial re-expansion of the right lung. Note the striking similarity to Figure 2.

from the right pleural cavity, but repeated subsequent aspirations were necessary in order to keep the dyspnea under control. Because it was felt that the adhesion shown in the roentgenogram (Fig. 3) might play some part in preventing closure of the perforation in the lung, thoracoscopy was performed by Dr. M. D. Tyson on April 11, 1936, and a cautery pneumolysis was done, severing the adhesion. Subsequent to this procedure, the patient's condition showed progressive improvement and the lung partially re-expanded (Fig. 4). It was at this examination that the large bleb on the right upper lobe was noted (Fig. 5). The patient was so much improved symptomatically

that he refused to remain in the hospital and was discharged against advice on April 24, 1936.

He returned to work and felt well until May 15, 1936, when he had a fifth attack characterized by dyspnea and cyanosis. He was readmitted to the hospital on May 16, 1936, in essentially the same condition as on the first admission, except that the symptoms were somewhat less severe. The roentgenogram taken at this time is reproduced in Figure 6.

Because of the frequent recurrence of the attacks of spontaneous pneumothorax, it was considered advisable to excise the emphysematous bleb as the presumable cause of the pneumothorax. Accordingly, this operation was performed by Dr. M. D. Tyson on May 23, 1936.

The pathological report by Dr. R. E. Miller was as follows: "Study of numerous sections reveals no definitely identifiable lung substance. The only feature suggesting the association of this specimen with the lung is the presence of a great many macrophages filled with black, carbon-like pigment. Elastic tissue stains reveal a very small amount of elastic tissue but none in any position to suggest any alveolar arrangement. No bronchial structures are seen. Two types of surface are seen in the section; one, which is interpreted as being the original pleural surface, has underlying it a broad band of dense hyalinized fibrous tissue. No covering is apparent and there is no infiltration of this region. Opposite this surface is one which bears a small amount of inflammatory exudate in spots. Adjacent to this surface there is abundant infiltration by eosinophiles, and a few polymorphonuclear leukocytes and scattered small accumulations of lymphocytes. There are some occluded small arteries. Vascular channels are numerous and there are some brown pigment filled phagocytes suggesting that there has been hemorrhage into the tissues."

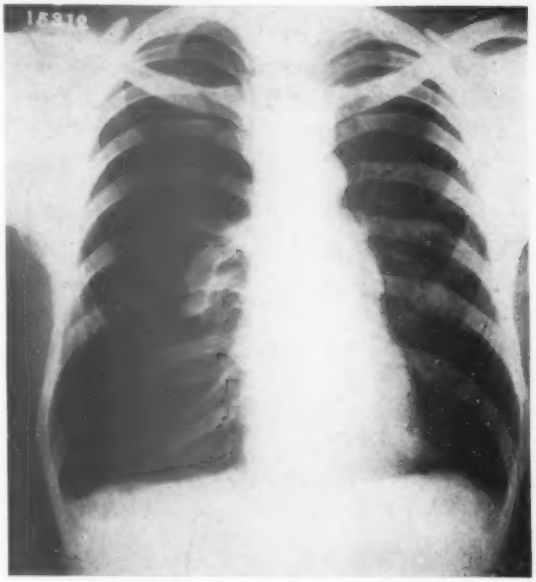

Fig. 6. Right pneumothorax (fifth attack). Another adhesion has formed.

Fig. 5. Enlargement of Figure 4.

The patient made a satisfactory recovery and has had no further attacks to date.

Comment. This patient has had five attacks of spontaneous pneumothorax in three years. An unusual feature of the case is the demonstration on the roentgenogram of the emphysematous bleb which is the presumable etiologic factor. The presence in the pathological specimen of fibrous tissue and anthracotic pigment and the absence of any bronchial structures justify a

diagnosis of emphysematous bleb rather than solitary lung cyst. Operation was performed for the removal of the emphysematous bleb. The surgical aspects of the case and the subsequent follow-up will be reported at a later date by Dr. M. D. Tyson.

I am indebted to Dr. F. S. Eveleth of Concord, N. H., for permission to use the films reproduced in Figures 1 and 2.

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A ROENTGENOLOGICAL STUDY OF THE HEART SIZE IN ATHLETES*

By HUGO ROESLER, M.D.
PHILADELPHIA, PENNSYLVANIA

THE rapidly changing attitude of cardiologists towards the value of the roentgenological method in the study of the heart and heart size is perhaps best expressed by the following two citations. Sir James Mackenzie[6] wrote as late as 1920: "Indeed, I am doubtful if an x-ray examination of the heart has ever thrown the slightest light on any cardiac condition." But in 1936 John Parkinson[8] says in his Lumleian Lecture: "Percussion had to serve in the past, and it may still serve as a crude expedient in certain cases, but the best proof that it is to be extruded from our important and growing number of clinical and laboratory methods is the fact that it is sterile. The tokens of sterility are upon it. Nothing has been added to medical knowledge or progress through cardiac percussion since the beginning of this century, and in the light of X rays it will shrink into obsolescence."

The following case reports will illustrate the fact that the heart of a healthy athlete may attain a size which is regarded as being at, or slightly above, the upper limits of normal and that a diminution in size may take place subsequent to discontinuation of the training.

The following abbreviations will be used for the different diameters: L for oblique, B for broad, T for transverse, Th for transverse thoracic, drawn at the level of the costodiaphragmatic sinuses. L×B is given as suggested by Moritz; this product is proportionate to the area.

CASE REPORTS

CASE I. Aged thirty-six. Had measles in childhood. Fourteen years of skiing, ice skating, bicycling and high mountain climbing. Feels well. The height is 184 cm. and the weight 86 kg. Strong muscular build. The apical thrust is hardly felt. The heart sounds are clear, there is no basal accentuation. Rate 64 per minute, blood pressure 130/80. The orthodiagram is shown in Figure 1.

CASE II. Aged twenty-one. Had pneumonia at the age of nine and tonsillitis at the age of

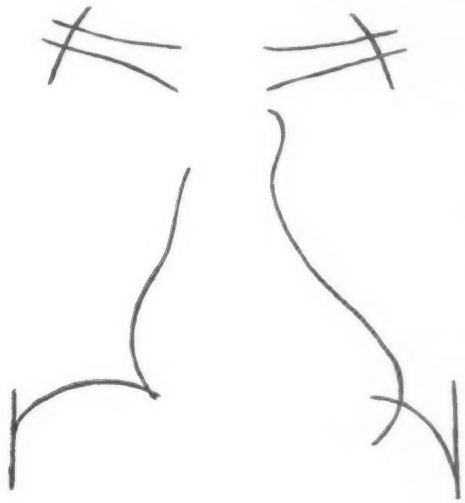

FIG. 1. Case I.

L	*B*	*L*×*B*	*T*	*Th*
15.2 cm.	10.4 cm.	158.1 cm.²	14.4 cm.	23.7 cm.

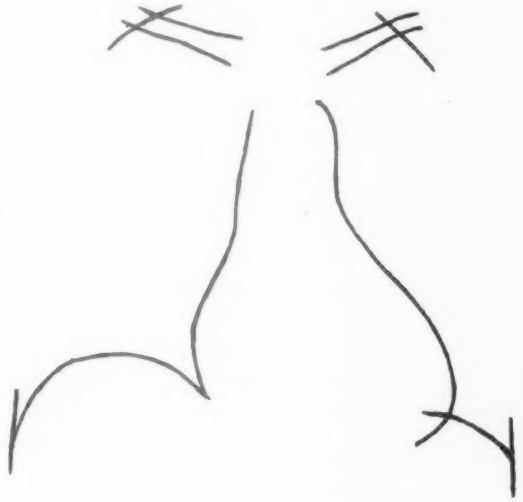

FIG. 2. Case II.

L	*B*	*L*×*B*	*T*	*Th*
14.8 cm.	11.5 cm.	163.3 cm.²	14.2 cm.	26.8 cm.

* From the Department of Radiology, Temple University School of Medicine, Philadelphia.

eleven. Seven years of football, baseball, wrestling and track. Feels well. The height is 170 cm. the weight 79 kg. and the chest circumference (expiration) 92.5 cm. Strong muscular build. The apical thrust is just palpable, slightly outside of the midclavicular line. The heart sounds are clear, P2 is moderately loud. Rate 58 per minute, blood pressure 118/78. The orthodiagram is shown in Figure 2.

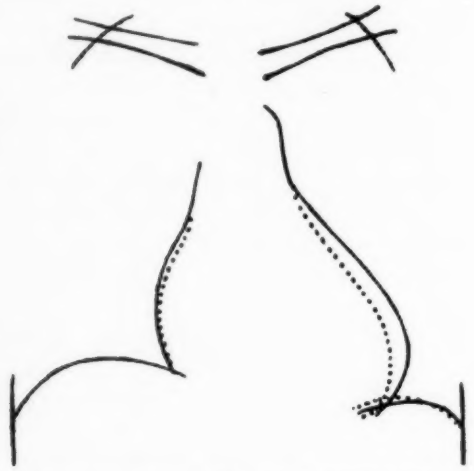

FIG. 3. Case III. The solid line tracing was taken during the training period, the dotted line tracing after athletic activity had been discontinued for two years.

	Dec. 1924	Oct. 1931
L	14.4 cm.	13.7 cm.
B	11.2 cm.	10.5 cm.
L×*B*	161.3 cm.^{2}	130.2 cm.^{2}
T	13.6 cm.	12.4 cm.
TH	24.3 cm.	24.4 cm.

Identical findings were present at three examinations in the course of eight months.

CASE III. The age was seventeen and twenty-four at the occasion of the two examinations. No infections since childhood. Three years of ice hockey (at that time the first examination was made). Then five years of training; no athletic activity for two years (at that time the second examination was made). Feels well. At age twenty-four the height is 166 cm. and the weight 67 kg. Well built. The heart sounds are clear. Rate 76 per minute, blood pressure 125/75. The two orthodiagrams, taken at an interval of seven years, are shown in Figure 3.

CASE IV. Aged twenty-two. Tonsillitis six months ago, followed by tonsillectomy. Eight years of football, baseball, hockey. Feels well. The height is 167.5 cm., the weight 87.3 kg. and the chest circumference (expiration) 98.7 cm. Stout, athletic build. The apical thrust is just palpable, 10.5 cm. to the left of the midline. There is a short systolic apical murmur which is not transmitted. P2 is not accentuated. Rate 72 per minute, blood pressure 138/82. The two orthodiagrams, taken at an interval of four weeks, are shown in Figure 4.

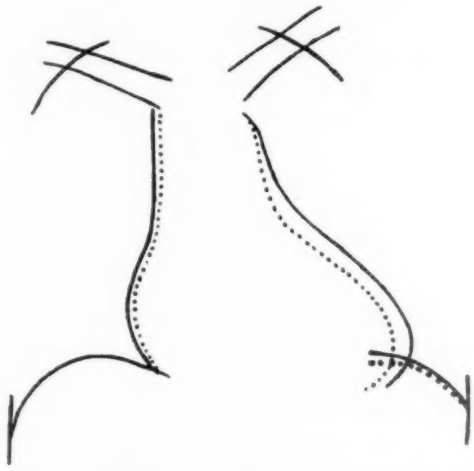

FIG. 4. Case IV. The solid line tracing was taken during the training period; the dotted line tracing after athletic activity had been discontinued for a period of four weeks.

	Sept. 1933	Oct. 1933
L	15.7 cm.	14.1 cm.
B	10.4 cm.	9.7 cm.
L×*B*	163.3 cm.^{2}	136.8 cm.^{2}
T	15.2 cm.	13.7 cm.
Th	23.6 cm.	23.9 cm.

DISCUSSION

A rough comparison of the cardiac silhouettes with the respective chest areas as well as the absolute figures proves that we are dealing in all 4 cases with hearts of considerable size. There is no history of significant infection. The clinical findings are normal and so is the functional state. Hearts of this size are by no means a common occurrence. They must, of course, be evaluated in connection with the total muscular development, which was exceptionally good in these cases, and most probably with the type of athletic activity; this is discussed later. The regression of heart size following cessation of training

cannot be doubted, the differences in the silhouettes definitely exceeding the possible technical error.

That the present status of roentgenological heart measurement with its usual limitation to one plane only is not satisfactory and that the goal of all measurement is the determination of the volume of the heart, I have pointed out previously.[10] The orthogonal projection in the anterior view, however, permits of an approximate crude evaluation of the heart size provided that the chest is symmetrically and proportionately built. Many athletes have a rather slow heart rate during the period of training. The amplitude of pulsations along the silhouette increases correspondingly and the figures for the systolic and diastolic size respectively reveal a significant difference, as I have shown.[11] For purposes of comparison, orthodiagraphic tracings which depict the diastolic phase may therefore reveal less numerical differences than teleroentgenograms which were taken with short exposure but without consideration of the phase of the cardiac cycle.

Moderate degrees of ventricular hypertrophy do not appreciably alter the size of the cardiac silhouette, though they may alter its shape. Excessive degrees of hypertrophy occur only with clinically easily recognized disease entities and will, even without associated dilatation, influence both size and shape of the silhouette.

Heart size will be discussed in reference to the ventricles. Isolated right atrial enlargement is exceedingly rare. Left atrial enlargement is typically associated with certain cardiac lesions and both are detected easily by roentgen examination. Heart size will be further discussed only in connection with prolonged, strenuous, competitive exercise.

In modern times, interest as to the possible influence of athletic activity begins in 1899 when Henschen[3] stated that he had found, by clinical methods, enlargement of the heart in natives of Lappland who were accustomed from childhood to cover long distances by ski. Such an enlargement, he believed, took place in normal healthy people with excessive exercise only and should be looked upon as a physiological process of adaptation. Other investigators thought that the heart muscle truly gained in bulk and certain animal experiments were cited to support this concept. A third group holds that the heart size in athletes is entirely normal and in good correlation with the development of the body and particularly of the muscular system. Reference is made to the writings of Dawson,[1] Deutsch,[2] Rautmann,[9] Roesler[12] and Steinhaus;[13] the contributions of these authors contain many valuable references on the subject.

Enlargement of the heart is looked upon differently by the physiologist, who may speak of a normal process of adaptation, and by the clinician, who looks upon this condition as a potential source of weakness of the contractile power of the muscle. It is likely that the study of the heart of the healthy athlete or hard working manual laborer will bring together the two slightly estranged brothers, the physiologist and the clinician.

The statements as to the findings of heart size after prolonged physical activity (military service, heavy manual labor, athletics) are greatly at variance. Those who claim enlargements seem to have often come to this conclusion either because hearts which were not normal to begin with were included, or because they compared their figures with certain standards without considering the total physical development. Often, too, average figures only were considered instead of the range of variation. And finally it is conceivable that a heart which was originally under size will develop to normal size, under the influence of training.

Rautmann[9] has stressed the importance of the type of athletic activity. Dynamic exercises can be subdivided into tests of speed, where efficiency in locomotion is needed in a given unit of time; and into tests of endurance, where less work is

accomplished in the unit of time, and a demand for efficiency in effort is made upon the muscle unit. In the former group belong short distance running, tennis, boxing, fencing. In the latter, skiing, rowing, cycling, swimming and running for long distances. Here a great capacity of the heart for a prolonged increased stroke volume is demanded. In the former group (tests of speed) the roentgenological heart size is, for practical purposes, always found to be normal. In the latter group (tests of endurance) a percentage of healthy athletes show a tendency to relatively larger silhouettes; nearly always, however, still within the norm, if sufficient correlation factors are considered. It must be pointed out, however, that static characteristics of the body, such as weight, chest circumference and the like do not have too great a statistical significance (Roesler[12]). Thus marathon runners, bicycle riders, oarsmen, skiers, and to some degree swimmers, mountain climbers, ice hockey players and ricksha pullers are the groups where the average heart size is relatively high and where single cases reach or just surpass what one might call the upper limit of normal.

It is not uncommon to observe during the period of severe training that the heart shadow increases moderately in size during the course of four to six weeks and recedes at about the same rate following cessation of training. Whether the process underlying the increase in heart size is only due to a stretching of the muscle fibers or whether there is also a thickening has not been decided. It is of fundamental importance, in this connection, to realize that single or numerous feats of physical activity may well cause an enlargement in the presence of a diseased heart muscle. This applies particularly to acute infections, but also to chronic infections or to those which have healed but left some damage. It was conclusively shown by Kaufmann's roentgenological and clinical studies that healthy soldiers who had undergone most strenuous efforts during the World War for a period of two and a half to three and a half years revealed a normal heart size; while a number of those who had gone through repeated infections revealed cardiac enlargement; these men had neither hypertensive nor valvular disease.

The presence of a fairly large "borderline" cardiac silhouette in an athlete may or may not have clinical significance from the viewpoint of both diagnosis and prognosis. This cannot be decided by the roentgenological method.

Further progress in knowledge might be expected from anatomical studies. A number of prerequisites ought to be fulfilled so that such a study may be of definite value. The individual in question should have been studied during life time so that significant data would be available, such as history of infections, blood pressure, etc. Physical activity should have been continued within a short time of death and the latter event should have occurred rather suddenly, for instance due to an accident or suicide. The anatomical examination must determine the body weight and heart muscle weight and the shape of the heart. A microscopic examination of the coronary arteries and of the heart muscle is a *conditio sine qua non*. One will realize that an opportunity for such a study will rarely be available. The pathologist Kirch requested many of his colleagues to send him the hearts of athletes who had suddenly died and on whom an autopsy had been performed. Including cases of his own and from the literature, he analyzed the hearts of 26 athletes who died during full physical activity and most of them instantaneously. He concluded that 14 instances revealed evidence of either definite or probable cardiac hypertrophy.

A critical analysis of this material shows that 7 cases should be discarded, 6 because of the presence of definite heart disease and 1, a woman, because of a recent delivery. Of the remaining 18 cases, there are figures for both heart weight and body weight available in 8 cases. In some of these an increase in the heart weight was as-

sumed to be present because the average figures were exceeded but this is open to criticism. Neither blood pressure readings taken during life, nor microscopic studies of the heart musculature are stated for most of these 8 cases. In assuming that these findings were normal, there seem to be available 3 anatomical instances of cardiac hypertrophy in athletes, with an average total heart weight of 457 grams and an average heart muscle weight of 377 grams. Kirch gives as average normal figures 345 and 282 grams respectively. Other authorities, however, consider 310 grams as an adequate average heart muscle weight for physically active and well-developed persons. These hearts were not globular in appearance but had an elongated shape. This seems to be nicely expressed in Figures 1, 2, and 4.

SUMMARY

Four cases are reported and it is demonstrated (1) that the heart in healthy athletes may occasionally reach a size which justifies the diagnosis of slight enlargement, and (2) that a diminution may take place after cessation of training.

Rautmann's concept of tests of speed and tests of endurance is given in relation to a possible cardiac response. Kirch's anatomical studies on the hearts of athletes are cited and critically analyzed.

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CARDIODYNAMICS IN RELATION TO THE ANALYSIS OF THE CARDIAC CONTOUR

By MARCY L. SUSSMAN, M.S., M.D.
Associate Radiologist to The Mount Sinai Hospital (Service of Dr. Leopold Jaches)
NEW YORK CITY

INTRODUCTION

FOR some time a complete roentgen examination of the heart has included an analysis of the cardiac contour for the determination of individual chamber enlargement. This has yielded more useful information than the exclusive use of the older method of describing cardiac measurements and configurations as characteristic of, or consistent with, certain disease conditions. It would appear timely to review the pathologic basis for the roentgen criteria of chamber enlargement, particularly of the ventricles, and to elaborate upon the responsible physiological mechanisms. This will provide an approach to the better correlation of the roentgen findings with the functional status of the heart during life, and with its anatomic appearance post mortem.

ANATOMY OF THE VENTRICLES

There is anatomic justification for dividing each ventricular cavity into two segments, the inflow and outflow tracts (Kirch[9]). The inflow tract is that segment between the venous ostium and the apex; the outflow tract is that segment between the apex and arterial ostium. In the right ventricle (Fig. 1, B), then, the inflow tract is situated posteriorly and is bounded by the posterior wall, the diaphragmatic surface of the ventricle and the adjacent portion of the septum. The outflow tract is situated anteriorly and is bounded by the anterior wall of the ventricle and the anterior larger portion of the septum. In the left ventricle (Fig. 1, C) the tracts are not so clearly separated, but in general the inflow tract from the mitral valve to the apex is situated posteriorly, and is formed by the posterior wall of the ventricle and the posterior portion of the septum; the outflow tract lies anteriorly and is formed by the anterior wall of the ventricle and the anterior portion of the septum. The muscle about the root of the aorta—the deep bulbospiral muscle (Robb[15])—is particularly well developed and forms virtually a separate muscle layer. These tracts are easily studied in waxed heart preparations, a collection of which Dr. L. Gross* has very kindly made available to me in connection with the present report.

The structure of the cardiac muscle differs as it forms the walls of these tracts. The wall of the inflow tract segment of each ventricle is markedly trabeculated, while the wall of the outflow tract is smooth. This arrangement naturally suggests a difference in function of the two segments of the ventricles.

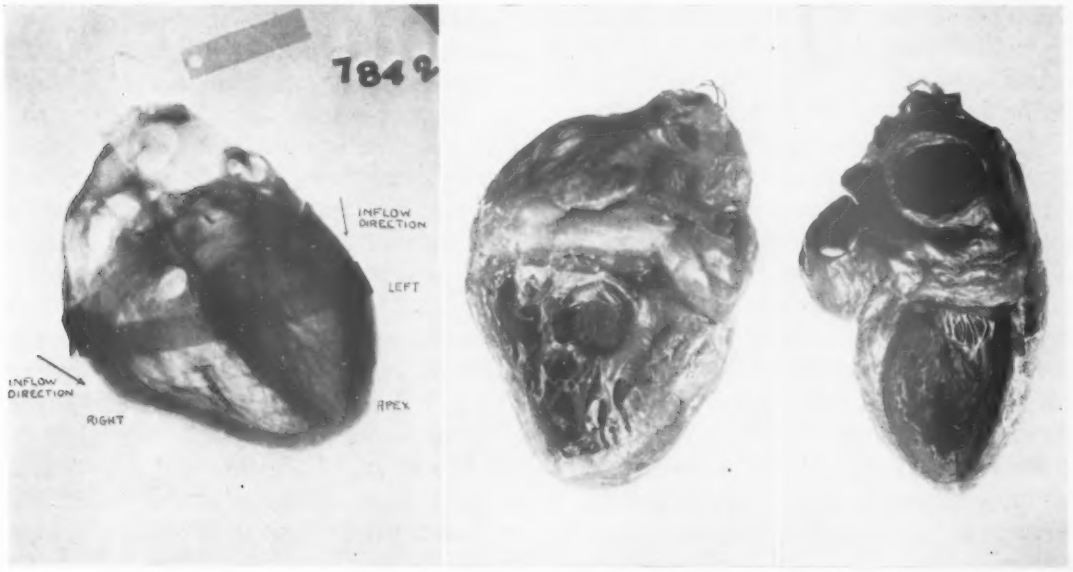
PATHOLOGIC PHYSIOLOGY OF THE VENTRICLES

Starling[19] and his coworkers have demonstrated by means of a heart-lung preparation that the immediate response of a ventricle to a demand for an increased output of blood is dilatation. They state, in effect, that the work done by a contraction is proportional to the initial length of the muscle fiber, or in other words, to the diastolic volume of the ventricle. Prolonged dilatation ultimately leads to muscle hypertrophy. With a normally functioning cardiac musculature responding to increased chamber output as, for example, in hyperthyroidism, so-called athletes' heart, etc., hypertrophy is always preceded by dilatation. This type of response is called by Kirch tonogenic enlargement of the ventricle, following the nomenclature of Moritz. Kirch further offers the opinion that dilatation and hypertrophy begin in

* Dr. L. Gross, Director of Laboratories, The Mount Sinai Hospital, New York City.

the outflow tract of the ventricle and that the change is characterized primarily by a lengthening of this tract along with deepening and widening. This is the type of ventricular change commonly referred to as eccentric hypertrophy. Actually, the change in shape and size is primarily the consequence of dilatation, and the degree of associated hypertrophy frequently can not be determined by either clinical or roentgenological methods.

trophy actually exists. The experimental work of Rytand and Dock,[17] confirming that of Chanutin and Barksdale,[4] seems to indicate that it does. They define concentric hypertrophy of the ventricle as an increase in the volume and weight of its myocardial fibers caused by an increase in the width of the fibers. This is associated with a small ventricular cavity and a shortening of the total length of the fibers. Eccentric hypertrophy, on the other hand,



A B C

Fig. 1. Waxed preparation of a normal heart. A. Roentgenogram made with the heart in approximately the position it occupies in the body. B. Waxed normal heart with anterior surface of the right ventricle removed, to show the cavity of this ventricle. C. The left ventricular cavity.

With increasing dilatation of the left ventricle the outflow tract widens and lengthens and the septum bulges into the right ventricular cavity. The inflow tract remains relatively short but undergoes hypertrophy of its wall. The apex, which in large part is a segment of the outflow tract, often shows the greatest change, becoming round and wide. This change is associated with the fact that the apex is formed only by the superficial layers of the heart as they turn inward in a figure-of-eight fashion to form the papillary muscles.

There has been a question in the minds of some as to whether concentric hyper-

implies a parallel increase in the volume of the cavity and in the wall of the ventricle, the latter being due to lengthening of the myocardial fibers. The conclusions of these authors are of importance in the understanding of the various cardiac contours observed in practice. They state that:

1. In the presence of experimental renal insufficiency the heart of the rat reacts to hypertension with an unquestionable concentric hypertrophy of the left ventricle.

2. In a ventricle with constant contractile energy a given unit of shortening of the muscle fibers will expel a comparatively

large volume (at relatively low pressure) if the initial capacity is great, while the same amount of shortening will develop a greater endocardiac pressure, the initial capacity being small (with a smaller stroke output). In this way the concentric hypertrophy of hypertension (with greater endocardiac pressure) and the eccentric hypertrophy of hyperthyroidism (with larger stroke output) are understood.

3. The optimal initial size of the heart in hyperthyroidism, which must expel an increased minute output against presumably normal peripheral resistance,* must be greater (in both chambers) than in hypertension in which there is a normal output and an increased peripheral resistance.

4. When hypertension develops slowly it is unlikely that dilatation occurs at any time.

One must disagree with the statement that the optimal initial size of the heart in hyperthyroidism depends upon an increased minute output. The important factor is stroke output, since the minute output can be increased merely by increasing the rate of the heart. It is also unlikely that no dilatation at all occurs in hypertension; it is more likely, according to most authors,[6] that slight dilatation appears, followed immediately by hypertrophy.

Podkaminsky[14] offers an explanation of the appearance of concentric hypertrophy of the left ventricle in the human. He conceives of the inflow tract as being the actual driving force behind the expulsion of blood from the ventricle, whereas the outflow tract serves partly as a groove or channel through which the blood passes, although, in addition, he postulates an expelling function to this tract in the sense that it continues the forward motion of the blood. The apex is said to share in the function of the outflow tract, but serves, in addition, as a reservoir for the residual blood. These statements are speculative but are correlated with the trabecular structure of the inflow tract and the smooth walls of the outflow segment. In hypertension then, where there is an increase in the endocardiac pressure, Podkaminsky believes that the ventricular response is a hypertonus of the inflow tract with subsequent hypertrophy but no significant dilatation. Only when the hypertonus developed by the inflow tract is insufficient does a secondary dilatation of the outflow tract occur and finally a dilatation of the inflow tract. In the majority of cases a hypertensive heart does not dilate materially until muscle damage occurs although there are some few cases in which marked enlargement occurs without significant myocardial damage. The hypertrophy of the muscle of the left ventricle which occurs in response to increased endocardiac pressure is sufficient ordinarily to compensate if the coronary arteries are adequate and remain so. Pathologists are fairly well agreed that the pathological changes seen in the myocardium of hypertensive patients are not due to hypertension but to coronary artery disease (Levine[10]).

Myogenic dilatation (Kirch[9]) may be characterized as a progressive dilatation without proportionate hypertrophy. Anatomically myogenic dilatation is characterized by a marked increase in the width and depth of the ventricular cavity as contrasted to the increase in length in tonogenic enlargement. Myogenic dilatation is ordinarily associated with a diseased myocardium and is the response of the ventricle to the necessity for maintaining chamber output. The increase in diastolic volume must be progressive because the amount of effective muscle per unit of surface area is diminished by disease. Furthermore, compensatory hypertrophy is minimized because hypertrophied muscle has a greater oxygen need, which the often narrowed coronary arteries are unable to provide. Whether stroke output is of significance in this connection or not is difficult to determine, since Harrison,[8] for example, states that there is a normal stroke output in cardiac failure.

* The lowered diastolic pressure in human hyperthyroidism suggests a peripheral dilatation.

ROENTGEN CORRELATION

Right Ventricle. The outflow tract is represented roentgenologically by the pulmonic conus segment of the left cardiac contour and by the anterior surface of the right ventricle. The inflow tract is represented largely by the diaphragmatic surface of the ventricle, and is seen best in the left anterior oblique position. In this position, it is usually possible to differentiate the apices of the left and right ventricles by the method suggested by Nemet.[13] If the patient is rotated into the left anterior oblique position until the heart shadow is separated from that of the spine one can usually see roentgenoscopically, in deep inspiration, a notch occurring with each systole which differentiates the apices of the two ventricles.

Inflow tract enlargement is characterized by an increase in the diaphragmatic surface and by a bulge of the cardiac shadow to the right which is seen best in the left anterior oblique position. Often an angle is seen in the contour below and to the right of the shadow of the base of the aorta in this position (Fig. 4, arrow). This does not represent a true angle in the sense that it can be demonstrated as such on the anatomical specimen, but is more a prominence of the right ventricle where it meets and pushes the right auricle upward and to the right, magnified because of the distance of this point from the screen during roentgenoscopy. Demonstration of this angulation is said to be pathognomonic of an enlargement of the inflow tract of the right ventricle (Nemet[13]). It is evident that as the outflow tract widens and the apex rounds and widens, part of the diaphragmatic surface is made up of this structure.

Further evidence of inflow tract enlargement is available in the posteroanterior and lateral views. In the former, enlargement is shown by widening of the cardiac shadow to the right and by elevation of the vaso-atrial angle on the right upper cardiac contour: the latter is probably due to displacement of the right auricle by the enlarged right ventricle (Assmann[2]). In the lateral view, there is a diminution in the size of the retrocardiac space.

The changes seen roentgenologically due to outflow tract enlargement depend in a large measure on a rotation of the heart. In mitral disease, there is a rotation about a longitudinal axis so that the pulmonic conus segment of the left cardiac contour is increased in length as seen in posteroanterior and right anterior oblique positions. The point of division between conus and left ventricle is seen closer to the apex than normally. The conus segment itself which is usually concave becomes straightened or may bulge. There is a diminution in the retrosternal space as seen in the lateral view. The rotation may be explained in this case as in part due to the pressure of the enlarged pulmonary conus against the anterior chest wall. Since left auricular enlargement occurs early in mitral disease, I believe that the pressure of this structure posteriorly assists in the production of the cardiac rotation. This will also explain why the left auricle when enlarged is not commonly seen on the left cardiac contour (Assmann[2]). It is important to differentiate the pulmonic conus segment if possible from that due to the pulmonic artery. The latter is situated higher on the left cardiac contour immediately under the "aortic knob," bulges more and has a later systolic impulse.

In some cases of right ventricular enlargement, the heart does not rotate on a longitudinal axis. In emphysema, for example, this is probably due to the fact that the deep chest allows more room for the anterior dilatation of the outflow tract. In the case of the right ventricular hypertrophy of congenital pulmonic stenosis with patent interventricular septum defect, I believe the absence of left auricular enlargement to be a factor, along with the fact that marked hypertrophy of the inflow tract also occurs. In both of these illustrations, there is no bulge in the pulmonic conus segment. The apex of the right ventricle widens and extends to the left producing in the case of the congenital lesion

the "coeur en sabot" configuration (Fig. 3). The lengthening of the outflow tract is manifested by a change in its direction so that it appears oblique in the posteroanterior view rather than almost vertical, as it normally does. Roentgenoscopy in the left anterior oblique position, by demonstration of the notch and the size of the diaphragmatic surface of the right ventricle, clearly demonstrates that the enlargement to the left seen in the posteroanterior view is actually due to the enlargement of the right ventricle.

Left Ventricle. Changes in the two tracts of the left ventricle are not as easy to differentiate because their longitudinal directions are approximately parallel, whereas in the right ventricle the two directions are more at right angles. Dilatation and hypertrophy of the outflow tract is shown by lengthening and widening. In other words, there is moderate enlargement to the left, the apex is displaced downwards, is pointed and shows to a greater degree in the gastric bubble than normally. Increasing dilatation is shown by further enlargement to the left and a rounding of the apex, as well as by a bulging into the retrocardiac space as seen in the left anterior oblique position, particularly in the lower contour at and near the apex (Arkussky[1]). Hypertrophy of the inflow tract is shown by a rounding of the upper left ventricular contour without increase in size to the left, and by elevation of the conus—left ventricle junction on the left cardiac contour. The apex is seen above the diaphragm in such cases. This rounding of the left ventricular contour is also seen posteriorly in the left anterior oblique position. With added dilatation the apex is broadened and the whole lower left cardiac contour is also rounded. With dilatation of the inflow tract marked enlargement to the left and upward is seen in the posteroanterior view, as well as an encroachment into the retrocardiac space in left anterior oblique and lateral views. This is the condition in myogenic dilatation.

Left Auricle. When the left auricle enlarges, it does so posteriorly, upwards and to the right. Evidence of enlargement of this chamber is indicated, therefore, by the appearance of its outline on the upper right cardiac contour in the posteroanterior view, rarely on the left cardiac contour between the conus and the left ventricle, elevation of the left main bronchus and displacement and compression of the esophagus posteriorly and to the right (Schwedel[18]).

Right Auricle. Enlargement of this chamber occurs to the right, upwards and posteriorly. It is difficult to demonstrate with certainty because it is often impossible to differentiate its shadow from that of the right ventricle. An enlargement of the heart shadow to the right beyond the midclavicular line almost surely indicates right auricular enlargement and even slighter degrees of enlargement to the right may be so interpreted in many cases. In the lateral view a shadow due to an enlarged right auricle often is seen extending into the posterior mediastinum just above the diaphragm, but which does not displace the esophagus. In the left anterior oblique view, a bulge in the upper right cardiac contour is also suggestive evidence. Enlargement of the right auricle is more often assumed, however, than actually demonstrated.

The description of the changes due to auricular enlargement has been made very brief since the subject has been exhaustively described in the literature (see, for example, Assmann[2]).

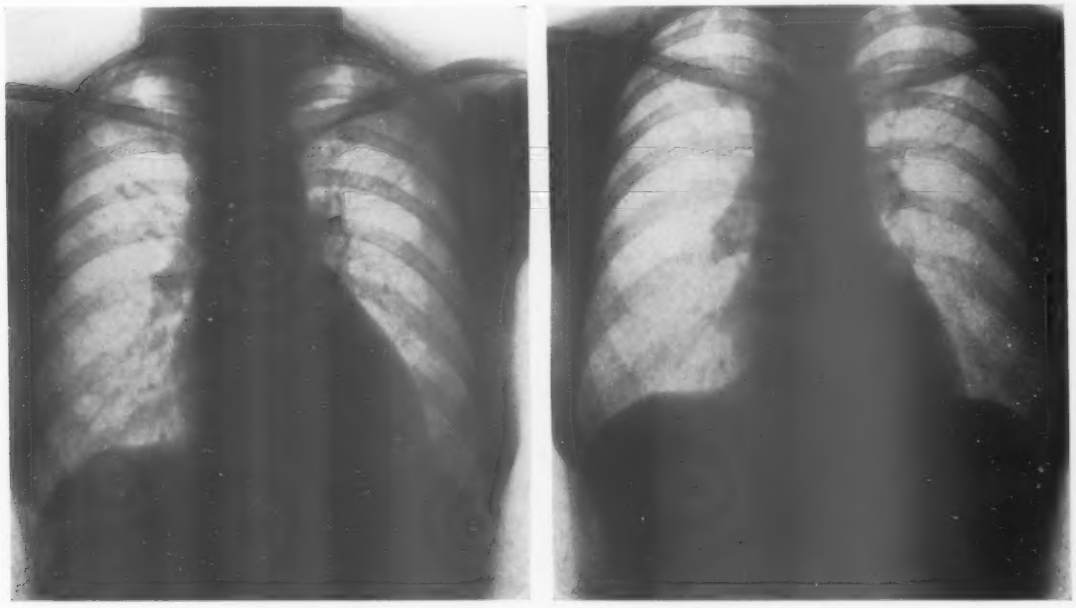
ILLUSTRATIVE CASES

Case 1 (No. 392228). A housewife, aged thirty-five, entered the Hospital with a typical history of hyperthyroidism of three years' duration. The heart was over-active and showed slight enlargement to the left. The sounds were of good quality with a soft apical systolic murmur, A2 louder than P2 and accentuated. The rhythm was regular, the rate 120. The blood pressure was 136/80. The basal metabolic rate was plus 40 (the average of three determinations) after receiving Lugol's solution, 3 minims daily, for one month. Electrocardiogram showed a sinus tachycardia and left ventricular preponderance.

A subtotal thyroidectomy was performed.

A roentgenogram of the chest before operation showed an enlargement of the heart to the left and downward (Fig. 2, A). Elongation of the left ventricle was well demonstrated, being out of proportion to the increase in the transverse diameter.

A re-examination of the chest was made four months after operation. The heart had definitely diminished in size and now had a practically normal configuration.



A B

Fig. 2. Case of Graves' disease. A. Before operation. B. Four months after subtotal thyroidectomy.

Comment. Gladstone,[7] in 4 cases of Graves' disease, with an average basal metabolic rate of plus 33 per cent, found the average cardiac output was 8.1 liters per minute compared with a normal of 4.2, representing an increase of 93 per cent. These figures corresponded to a systolic output of 88 c.c. per beat in the cases of Graves' disease as compared with a 70 c.c. output in the average normal. The response of the left ventricle in the present case, to increased systolic output, was dilatation, manifested by lengthening and widening of the outflow tract. Four months after operation, the heart had returned to normal size and to virtually normal shape. It is possible that, with the removal of the cause for hypertrophy of the left ventricle, the muscle fibers return to normal size much as does a skeletal muscle under similar conditions. However, the more likely probability is that the elongation and widening of the left ventricle noted roentgenologically were due chiefly to dilatation and that this was the condition that receded on removal of the cause. There is no roentgenological method for determining the actual degree of hypertrophy involved.

This case did not illustrate a common finding in cases of Graves' disease, namely a bulge in the left upper cardiac contour. There is evidence to suggest that this finding is due to a dilatation of the pulmonic artery, which also recedes following cessation of thyrotoxicosis (Margolies, Rose and Wood[11]).

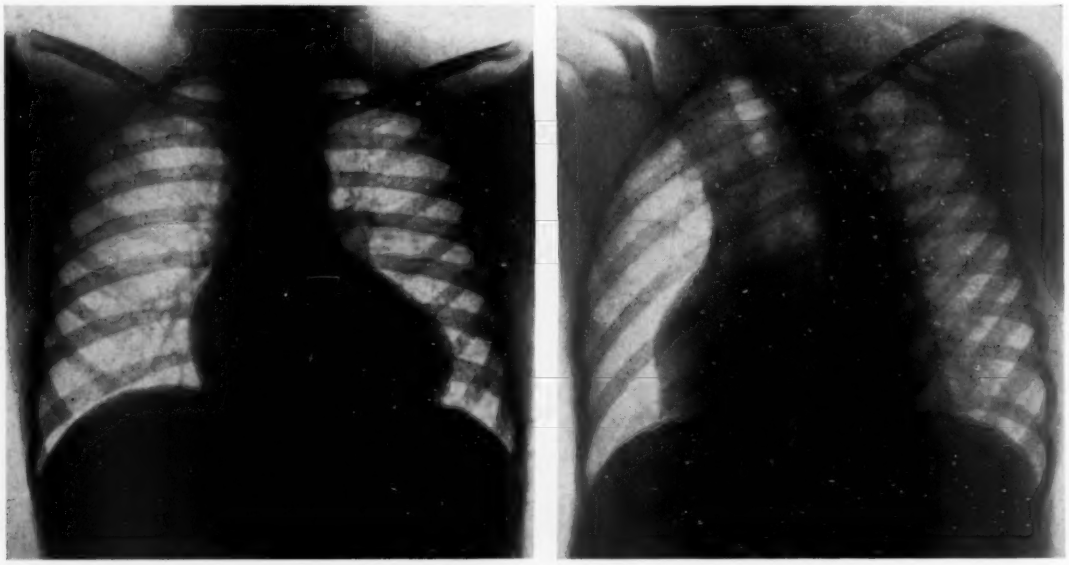
Case II (No. 345322). A boy, aged twelve, entered the Hospital with increasing blueness of the skin and mucous membranes, clubbing of the fingers and toes and old purpuric spots on the skin. The heart was enlarged to both sides; its rhythm was regular. There was a faint systolic murmur over the apex just to the

left of the sternum and an entirely separate, loud systolic murmur over the aorta. P2 was not accentuated. The liver was moderately enlarged. Blood examination revealed a fairly marked secondary polycythemia, the hemoglobin being 138 per cent. Electrocardiogram showed a left ventricular preponderance, T1 prominent and upright, T3 sharply inverted. There was high voltage in the main deflection; rate 120.

Roentgenograms of the chest (Fig. 3) showed a marked enlargement of the heart to the left with rounding of the lower left cardiac contour. There was also a slight elevation of the right vasoatrial angle in the posteroanterior view. In the left anterior oblique view, however, the roentgenogram demonstrated a marked widening of the diaphragmatic surface of the right ventricle and roentgenoscopy revealed, by the position of the apical notch, that the enlargement of the heart was chiefly due to the right ventricle, and that there was no elevation of the left main bronchus. Roentgenoscopy in the right anterior oblique position showed no deviation of the esophagus. The examination, therefore, indicated marked right ventricular enlargement in both inflow and outflow tracts without significant enlargement of any of the other chambers.

Post mortem revealed a patent interventricular septal defect, pulmonic stenosis, marked hypertrophy of the outflow and inflow tracts of the right ventricle, patent foramen ovale and dextroposition of the aorta (tetralogy of Fallot).

Comment. The roentgen evidence definitely indicated a right ventricular hypertrophy and dilatation. The "coeur en sabot" configuration and absence of a bulge in the pulmonic conus region was explainable by a rotation of the heart on the transverse axis as described in the text above. The absence of left auricular enlargement definitely excluded mitral disease. The absence of an enlargement of the pulmonic artery on roentgen examination was confirmed by post-mortem findings. This placed the point of increased resistance at the pulmonic valve. The pulmonic stenosis gave rise to a markedly increased intraventricular pressure in the right ventricle so that blood passed from the higher pressure side to the lower pressure side, that is, from right to left ventricle through the patent interventricular septal defect, giving rise to cyanosis and marked right ventricular hypertrophy. The dextroposi-



A B

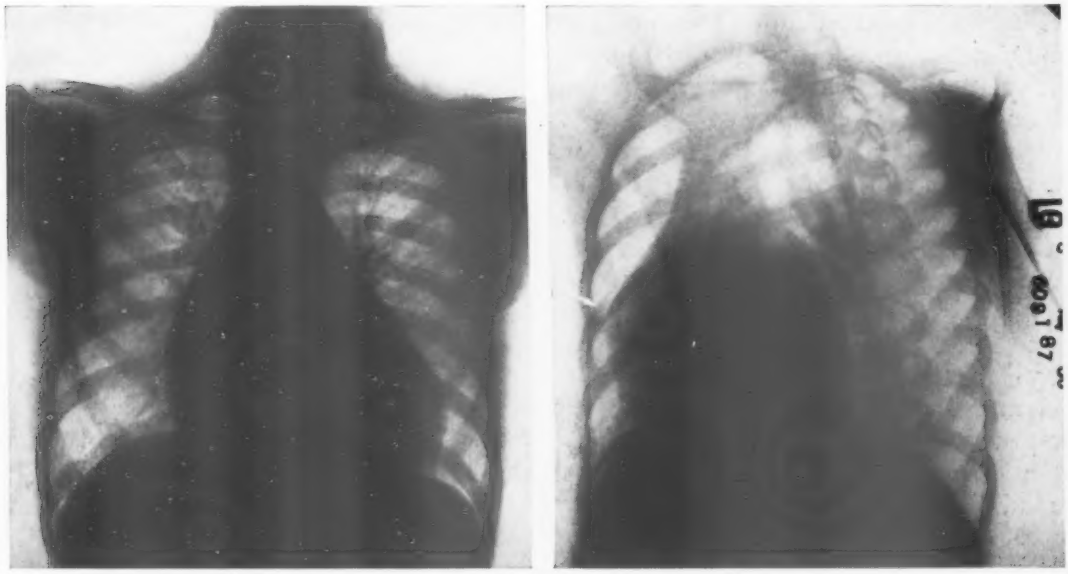
Fig. 3. Congenital heart disease—tetralogy of Fallot. Posteroanterior (A) and left anterior oblique (B) positions.

tion of the aorta was not clearly demonstrated roentgenologically.

Case III (No. 396714). A boy, aged fifteen, entered the Hospital complaining of progressive dyspnea and palpitation on exertion for two years. The past history included no definite evidence of rheumatic fever.

The heart was moderately enlarged to the left. The apex beat was diffuse. There was a rumbling presystolic and a blowing diastolic murmur at the apex. There was also a loud blowing diastolic murmur over the lower sternum and at Erb's point. The blood pressure was 120/75. Electrocardiogram revealed a right ventricular preponderance and an inversion of T_3, suggesting an enlargement of the right ventricle.

Roentgenographic examination showed the cardiac shadow to be enlarged to the right and left. There was a straightening of the left upper cardiac contour with a bulge in the region of the pulmonic artery and straightening and elongation of the pulmonic conus region. The junction of the pulmonic conus and left ventricle on this contour was displaced downward but the apex of the left ventricle was in the usual position above the diaphragm. On the right cardiac contour, the vasoatrial angle was elevated and there was a suggestion of the double contour commonly seen when an enlarged left auricle protrudes on the upper right cardiac outline. Roentgenoscopy in the right anterior oblique position showed a compression and posterior displacement of the esophagus. Examination in the left anterior oblique position showed a marked enlargement of the diaphragmatic surface of the heart. The position of the apical notch indicated that this was due to an enlarged right ventricle, confirmed by the prominence of the upper right cardiac contour with more or less angulation (arrow, Fig. 4). The position of the apical notch in relation to the retrocardiac widening indicated that there was, in addition, enlargement of the left ventricle of moderate degree with some elongation. There was elevation of the left main bronchus. In the posteroanterior view, the aortic shadow was seen to be smaller than normally.



A B

Fig. 4. Mitral stenosis and insufficiency. Possible additional aortic valvular disease. Posteroanterior (A) and left anterior oblique (B) positions. Arrow indicates angulation on upper right contour indicating right ventricular enlargement.

Comment. The roentgen findings indicated the presence of a marked enlargement of the left auricle and of the right ventricle in both the inflow and outflow tracts. There was also evidence of moderate dilatation and hypertrophy of the left ventricle. These findings indicated a lesion producing left auricular and right ventricu-

lar enlargement predominantly, that is, a mitral stenosis. The moderate enlargement of the left ventricle would be consistent with an additional mitral insufficiency or an aortic insufficiency. In the case of mitral insufficiency, it has been shown experimentally (Wiggers[21]) that the left auricular pressure rises during ventricular systole, instead of dropping as it usually does. For this reason, the ventricle fills more completely, increasing its initial tension and its diastolic size. Therefore the ventricle expels a larger tidal volume. The increased volume of blood is accommodated largely by an expansion of the left auricle and pulmonary veins but the pressure in the pulmonary circulation is not markedly increased. As a result, right ventricular changes are not so marked; in fact, experimentally, no significant rise in right ventricular pressure has been noted (Wiggers). The modification in the roentgen findings, when insufficiency is superimposed on mitral stenosis, consists in evidence of moderate dilatation and hypertrophy of the left ventricle, marked enlargement of the left auricle, but a less marked right ventricular enlargement. The pulmonary artery may be dilated. The dilatation of the left ventricle is sometimes marked in the region of the inflow tract so that an aortic configuration is simulated.

The circulatory adjustments, which occur in the presence of an aortic insufficiency alone, are due to the fact that there is a positive pressure in the left ventricle during all periods of diastole. Since, however, in the presence of a mitral stenosis alone, the left ventricular cavity is smaller, the effect of a superimposed aortic insufficiency does not tend to produce the cor bovinum usually associated with the latter condition. In general, it may be stated that the cardiac contours of these combined lesions depend largely on which lesion appeared first and which is more severe. From the practical point of view, it will be realized that the description of the changes in the individual chambers is of more significance clinically than the naming of the anatomic lesions. This is especially true since our theoretical discussion presupposes a normal myocardium, which is not usually present in these combined lesions. The importance of the diseased myocardium in heart failure in rheumatic valvular diseases has been stressed by Rothschild, Kugel and Gross,[16] especially in regard to the appearance of acute myocarditis. The demonstration of marked right ventricular enlargement, including inflow tract dilatation, does not necessarily have the grave prognostic significance here that it has in long-standing obliterative pulmonary disease or in a hypertensive heart. In the latter two conditions, Nemet[12] found such enlargement usually to indicate advanced cardiac insufficiency. In rheumatic mitral disease, on the other hand, definite enlargement can be seen with a fair or even good circulatory state, although in most cases with demonstrable inflow tract enlargement there is some evidence of impaired cardiac reserve. In this connection the recent report of Bland, Jones and White[3] is of interest. Along with the disappearance of physical signs in some cases of rheumatic heart disease, they have noted definite diminution in the size of the cardiac shadow. One of their illustrated cases also shows a change in shape from a typical mitral configuration to a contour which, one would judge, represents a dilated left ventricle. It appears probable that in the acute phase an edema of the leaflets of the mitral valve produces stenosis and insufficiency. Later, when the edema subsides, either a fairly normally functioning valve remains or an insufficiency; the latter will explain the rounded left ventricular contour with enlargement to the left.

CASES IV *a*, *b*, *c*, and *d*. Illustrating hypertensive heart disease.

(*a*) (No. 396946). A female, aged fifty-two, entered the Hospital complaining of nausea, headache and vertigo of four months' duration. Seven years before admission the patient was told that she had hypertension. For the past two years there have been recurrent episodes of edema of the lower extremities.

Significant cardiac findings included a moderate enlargement of the heart to the left as determined by percussion. The point of maximal impulse was nearly in the anterior axillary line in the 5th intercostal space. There were no murmurs. A2 was louder than P2 and was accentuated. The blood pressure was 190/100. There was moderate peripheral sclerosis.

Electrocardiogram showed a regular sinus rhythm, left ventricular preponderance, QRS slurred and of high voltage, Q3 large. These findings suggested muscle damage.

Roentgen examination (Fig. 5–1) showed a moderate enlargement of the heart to the left with rounding of the left ventricular contour. This was confirmed by examination in the left anterior oblique position, where an enlargement of the left ventricular contour into the retrocardiac space was noted. The evidence therefore suggested a concentric hypertrophy of the left ventricle with moderate dilatation. The latter was in conformity with the electrocardiographic evidence of muscle damage.

(*b*) (No. 360595). A male, aged fifty-three, entered the Hospital the first time with a history of a sudden onset of nausea, vomiting and precordial pain seven months before, with recurrent attacks since. Orthopnea and dyspnea were increasing.

The heart was found to be moderately enlarged to the left. P2 was louder than A2. There was a right pleural effusion, 3 liters of fluid being removed by thoracentesis. The liver was enlarged to three fingers' breadth below the costal margin. The blood pressure was 154/104. The electrocardiogram showed evidence of a

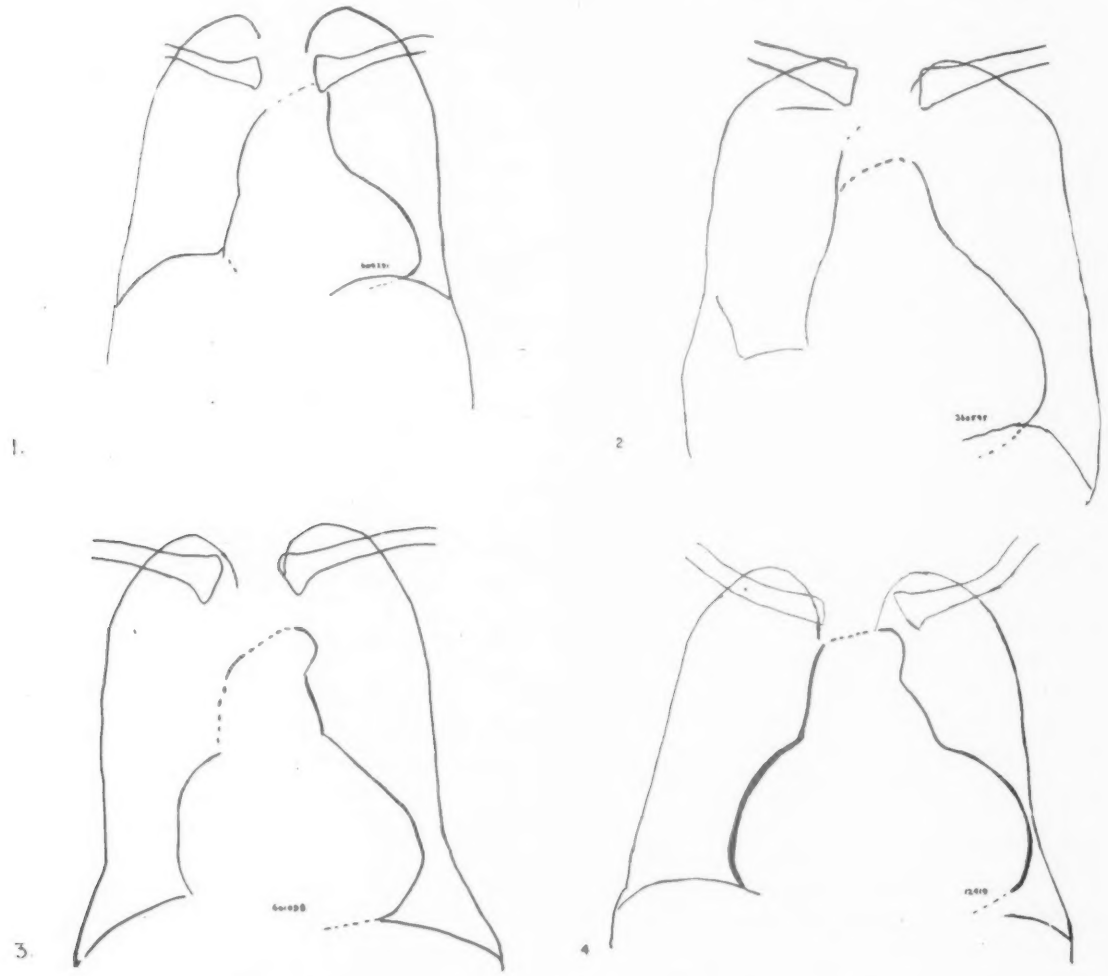


Fig. 5. Four cases of hypertensive heart disease (see text).

right ventricular preponderance, with low T waves in all leads. The curve suggested marked myocardial damage.

A roentgenogram at that time, only the report of which is available, showed enlargement of the heart to the left with a configuration suggesting an advanced mitral lesion. The clinical diagnosis at this time was coronary artery disease and mitral stenosis.

The patient re-entered the Hospital nine months later with increasing dyspnea and cough. There was a right pleural effusion; the liver was just palpable; and the cardiac sounds were poor. Blood pressure was 160/110. Complete roentgen study at this time (Fig. 5–2) showed evidence of hypertrophy and dilatation of the left ventricle: there was rounding of the left ventricular contour, elevation of the conus —left ventricle junction, and also an elongation of the ventricle. There was a straightening of the upper left cardiac contour and a broadening of the diaphragmatic surface of the heart as seen in the left anterior oblique position, indicating hypertrophy and dilatation of the outflow tract of the right ventricle, as well as dilatation of the inflow tract. The left auricle was enlarged, the esophagus being displaced posteriorly. These findings suggested a mitral insufficiency but the rounding of the left ventricular contour and elevation of the conus—left ventricle junction—was in keeping with a concentric hyptertrophy which would be anticipated due to the presence of hypertension. In the light of the clinical data one had to interpret the findings as indicating hypertensive heart disease with myocardial damage. The enlargement of the right ventricle suggested a fairly advanced form of the disease. The left auricular enlargement, however, suggested the presence of mitral insufficiency. It could not be determined with certainty whether this was due to organic mitral disease or to a functional mitral insufficiency depending upon the dilatation of the left ventricle. Vaquez[22] described the latter as due to outward displacement of the papillary muscles so that the chordae tendineae which connect them to the valves, are displaced eccentrically. They no longer have sufficient length to permit the valve curtains to come together during systole. In the presence of auricular fibrillation, the asynergic contraction of the auricle may also be a factor.

(*c*) (No. 389316). A male, aged sixty, entered the Hospital with a history of progressive dyspnea, palpitation and precordial pain for eight years. During the four days prior to admission he had suffered three attacks of suffocation lasting three to six hours each.

The heart was found to be enlarged to the left. The heart rate was 160. The blood pressure was 170/140.

Electrocardiogram showed auricular flutter and left ventricle preponderance. The QRS complex was of low amplitude, RS-T was elevated in lead IV. The auricular rate was 300, the ventricular rate was 140 to 180.

Roentgen examination (Fig. 5–3) showed enlargement of the heart both to the right and to the left. The left ventricular contour showed rounding and elevation of the conus—left ventricle junction, suggesting concentric hypertrophy. The enlargement of the left ventricle was marked and its contour suggested a myogenic dilatation in addition to the hypertrophy. The examination also showed a straightening of the upper left cardiac contour and an elevation of the atrioventricular angle on the right. This suggested an enlargement of the right ventricle which was confirmed by the usual findings of this condition in the left anterior oblique position. The findings therefore suggested dilatation and hypertrophy of both ventricles with myocardial damage. This was confirmed at post-mortem examination. A pulmonary emphysema was also found which might have accounted in part for the right ventricular hypertrophy. In this latter connection it may be noted that myogenic dilatation of the right ventricle may overshadow the anticipated hypertrophic response of this ventricle to emphysema because of the common coincidental occurrence of myocardial damage in older people.

(*d*) (No. 318689). A male, aged fifty, was known to have had hypertension (230/120) for at least two years previous to his first admission in 1930. At this time he was in cardiac decompensation, the signs and symptoms being those of right heart failure. His electrocardiogram showed low voltage, and inverted T1 and low T2. Roentgen examination at this time (Fig. 5–4) showed a marked enlargement of the cardiac shadow to the left and to a lesser degree to the right. The appearance suggested marked dilatation of both ventricles with marked hypertrophy of the left. The findings therefore indicated confirmation of the clinical impression of hypertensive heart disease with myocardial damage.

The marked dilatation of the ventricles in such cases is in part myogenic but is probably also related to the increase in the volume of circulating blood. Fishberg, Hitzig and King[5] indicated this possibility in pointing out that when infarction occurs in patients with previous heart failure, if failure predominates over shock, the volume of the circulating blood is increased, the venous pressure is elevated or normal and the flow of blood through the lungs is retarded.

Case v (No. 319650). A male, aged fifty-three, was admitted with a history of substernal oppression and dyspnea for five months previously. Three days before admission he had severe precordial pain which lasted all night. For six years he had dyspnea and palpitation on exertion. He consulted a physician, five days before admission, who found that the patient's systolic blood pressure was 200.

The fundal arteries were found to be erect and stiff, compressing the veins. There were hemorrhages and exudates throughout both fundi. The heart, by percussion, showed a marked enlargement to the left. There was no enlargement to the right. There was a blowing systolic murmur over the apex and axilla. P2 was not accentuated. The abdomen was distended. The liver could be felt down to the level of the umbilicus and it was tender and nonpulsating.

The blood pressure was 190/120. The urine showed albumin, hyaline and granular casts. Kidney function tests revealed evidence of a moderate impairment. Electrocardiogram showed a left ventricular preponderance. The T wave was inverted in all leads. The curve suggested coronary artery disease. Roentgenographic examination of the heart showed a very marked enlargement to the left. The shape suggested marked dilatation of the left ventricle, the rounding of its contour suggesting previous hypertrophy. In addition, there was a certain elongation, suggesting that part of the apparent dilatation might be due to hypertrophy. The aorta was dilated and tortuous. Roentgenoscopy showed no evidence to suggest enlargement of any of the other chambers.

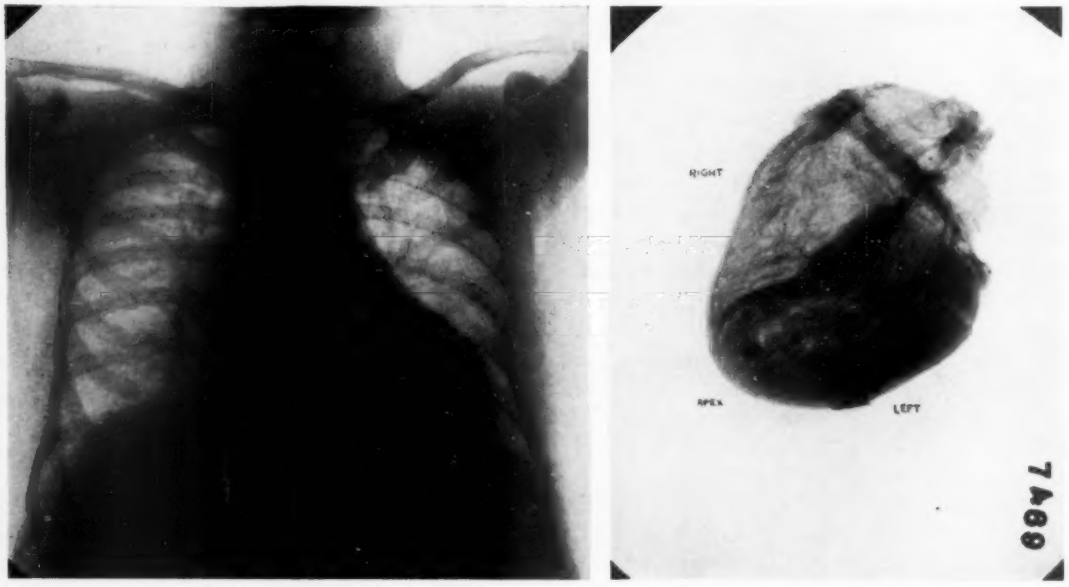
The correlation of clinical and roentgen evidence suggested coronary artery disease, involving chiefly the left ventricle, with moderate hypertrophy and marked dilatation, with hypertension on the basis of a chronic glomerulo-nephritis.

The patient died one month after entering the Hospital and post-mortem examination showed the following: The heart was markedly enlarged and weighed 850 grams. The left ventricle was enormously hypertrophied, its cavity being relatively small. The right ventricle showed only slight hypertrophy and dilatation although there was a moderate bulge in the region of the pulmonic conus. The lower third of the left ventricle anteriorly showed a dark colored area of softening which spread into the ventricular septum. This was due to a thrombosis of the left anterior descending coronary artery. There were old scars in the muscles of the right ventricle. The left auricle was not enlarged. The right auricle was dilated.

Comment. The enormous enlargement of the left ventricle demonstrated on the roentgen film (Fig. 6) suggested marked dilatation but the rounding of its contour, together with the position of the apex just above the diaphragm, indicated hypertrophy. Roentgenoscopy did not reveal any evidence of right ventricular enlargement so that the enlargement of the heart shadow to the left could be attributed entirely to the left ventricle. The marked widening of the left ventricle suggested a myogenic dilatation with preceding hypertrophy. This was in agreement with the finding of hypertension which was present even during the acute attack of coronary artery thrombosis.

A consideration of the roentgenogram of the present case, in relation to one made of the waxed heart (Fig. 6,B), shows a rather marked disproportion between the size of the ventricular cavity on this preparation as compared with that which might be expected from the film. The following factors may have some bearing: (1) The waxed heart is only an approximate representation of the actual size and shape of the heart. A certain amount of shrinkage and distortion is unavoidable during preparation. (2) The chest in this case was large so that there may be an unusual magnification of the cardiac shadow because of the distance of the heart

from the anterior chest wall. (3) The wide chest was also associated with an elevated diaphragm, which produces a large transverse diameter as seen on the roentgenogram. (4) A further, although remote, possibility in this case is associated with the area of myomalacia found anteriorly. It has been shown experimentally (Tennant and Wiggers[20]) that in ventricular systole there is a ballooning of the softened area of heart musculature. It is conceivable that such an area may appear larger during life than at post mortem and so modify the contour.



A B

FIG. 6. Myocardial disease. Roentgenogram of chest shown in comparison with one made of the waxed heart of this case.

It must be concluded then, that in the presence of an enlargement of the left ventricle it is often very difficult to determine the individual rôles of hypertrophy and dilatation roentgenologically, just as it was in the case of Graves' disease. Even a marked increase in the thickness of the ventricular muscle cannot explain the marked enlargement to the left which is sometimes observed. It must therefore be assumed either that there is present during life a dilatation of moderate degree which is not demonstrable at post mortem or that hypertrophy of the left ventricle, particularly of the inflow tract, produces a rotation of the heart on a horizontal axis so that its shadow extends farther to the left than normally. I think that this latter explanation is possible because in a case in which a calcified aortic valve was demonstrated roentgenologically and the direction of the outflow tract was thus definitely indicated the latter was nearly transverse. This means that with hypertrophy and only moderate dilatation, a marked enlargement to the left can occur.

SUMMARY

This review of the anatomy and the pathologic physiology of the ventricles has been given in an effort to make understandable the changes in the cardiac contour seen roentgenologically in various disease conditions. The changes in cardiodynamics depend on whether the cardiac musculature is healthy or diseased. When healthy, the response of the ventricle to an increased stroke output is dilatation of the outflow

tract followed ultimately by hypertrophy of the outflow tract and of the inflow tract. The response of a ventricle to increased endocardiac pressure with small stroke output is hypertrophy without dilatation, manifested primarily in the inflow tract. In the presence of a diseased myocardium, the ventricle widens in outflow and inflow tracts. The degree of hypertrophy depends in a large measure upon whether a disturbance in cardiodynamics was present previously or not. These principles were illustrated in an analysis of cases of Graves' disease, mitral disease, congenital cardiac disease, hypertension and myocardial disease.

It is believed that a knowledge of these principles will aid in the more useful interpretation of the cardiac contour. Such an analysis is also made necessary by the fact that so many cases do not conform to what the textbooks describe as "typical cardiac configurations."

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DRUGS AS AN AID IN ROENTGEN EXAMINATION OF THE GASTROINTESTINAL TRACT

THE USE OF MECHOLYL, PHYSOSTIGMINE, AND BENZEDRINE IN OVERCOMING ATONICITY, SLUGGISHNESS OF PERISTALSIS, AND SPASM

By MAX RITVO, M.D.
BOSTON, MASSACHUSETTS

IN THE roentgen studies of the stomach and intestines, spasm, atonicity, and sluggishness or absence of peristaltic activity are of frequent occurrence and add greatly to the difficulties of arriving at a correct diagnosis. To abolish spasm, belladonna and atropine are recommended by most authorities and have been widely employed. These drugs, however, have never proved effective and during recent years roentgenologists are generally agreed that little if any reliance can be placed in their efficacy. To combat atonicity and sluggishness of peristalsis, there was no agent in general use till 1927. At this time, Ritvo and Weiss[1] studied the action of physostigmine and found it to be of great value in ocercoming these difficulties. During the past nine years, in our clinics physostigmine has been routinely employed with success to increase tonus and peristalsis. The problem of abolishing spasm, however, remained unsolved until a year ago when Myerson and Ritvo[2] studied the effects of benzedrine on the gastrointestinal tract. This drug appears effective in combating spasticity of the stomach and intestines and holds promise of being a valuable aid to the roentgenologist. At the present time, the action of other drugs, in particular mecholyl, is under investigation in an attempt to find the ideal agents for our purposes. This paper will summarize briefly our experiences with the practical applications of these drugs.

A brief review of the physiology of the nervous control of the gastrointestinal tract is essential to the proper understanding of this subject. Unfortunately, the details of this fundamental and important topic have not as yet been clearly elucidated by physiologists. It is known that the autonomic nervous system, which exercises control over the stomach and intestines, is composed of two divisions, the sympathetic and the parasympathetic. The action of the sympathetic nerves is to decrease tonus and spasm; the parasympathetic nervous system increases tonus, peristalsis and spasticity. It is possible to stimulate or paralyze one portion or the other of the autonomic nervous system with resultant changes in the activity of the gastrointestinal tract. The roentgenologist can, by choice of the proper agent, play upon the sympathetic or parasympathetic nerves to cause variations in tonus, peristalsis, or spasm, and produce the changes desired to aid him in his studies. Normally, the two divisions of the autonomic nervous system are in a state of balance; disturbances of this equilibrium may be as important as stimulation or paralysis of one portion or the other. Some patients under ordinary conditions are suffering from overactivity of the sympathetic nerves, or sympathotonic, while others are para-sympathotonic. It must be borne in mind that these wide variations in the tonus and activity of the gastrointestinal tract are considered to be within normal limits, and changes which occur after the administration of drugs may vary according to the antecedent state of the organs. The emotions exert a powerful effect on the autonomic nervous system and the gastrointestinal tract rapidly reflects any change in mood. Fear, hate, excitement, in fact any violent emotion may cause spasm, atonicity, cessation of peristaltic activity, reverse peristalsis, and other important changes in the alimentary system; this factor must

also be taken into consideration in studying the effects of drugs. Drugs which cause changes similar to those of sympathotonus are called sympathomimetic, and in this group are ephedrine and benzedrine; agents such as mecholyl and physostigmine are parasympathomimetic. Atropine reduces the activity of the parasympathetic nerves.

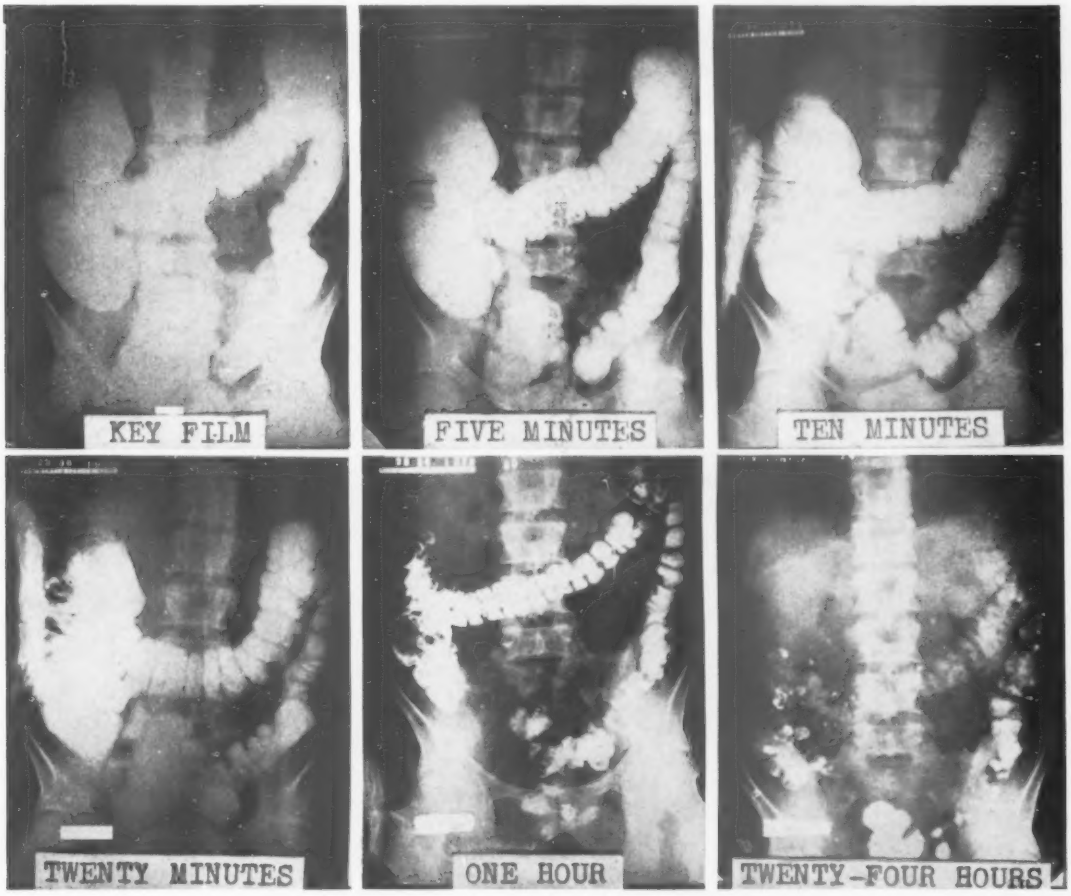

FIG. 1. *The effect of mecholyl on the colon.* The key film, before administration of the drug, shows a markedly dilated and atonic colon. Films at intervals after 30 mg. of mecholyl was administered subcutaneously show a very marked increase in tonus with narrowing of the lumen and increase in the number and depth of the haustrations. The twenty-four hour film shows extensive emptying of the colonic contents, whereas previously the patient had been markedly constipated.

DRUGS WHICH INCREASE PERISTALSIS AND TONE

The atonic stomach is frequently very difficult to examine roentgenologically. The opaque meal tends to collect in the lowermost portion of the stomach, the upper and middle thirds of the gastric lumen being narrowed and elongated. Pressure defects from the gas-filled colon, the spleen, and other adjacent organs are accentuated. It frequently is impossible to visualize all portions of the stomach and duodenum satisfactorily; and defects may occur without its being possible to determine whether they are the result of intrinsic disease, spasm, or pressure. If there is, simultaneously, absence or marked sluggishness of peristaltic activity, the difficulties of diagnosis are still further increased. Pressure over the stomach with the gloved hand and reassurance of the

patient to overcome nervousness or apprehension are helpful maneuvers and should always be resorted to for a reasonable period of time. When these methods proved unavailing, it was formerly necessary to repeat the examination after an interval of hours or days, with consequent delay and loss of time in completion of the roentgen studies. Now, however, it is usually possible, by giving the patient a dose of a suitable drug, to complete the studies at once. In the type of case under discussion mecholyl or physostigmine usually produces the desired effects.

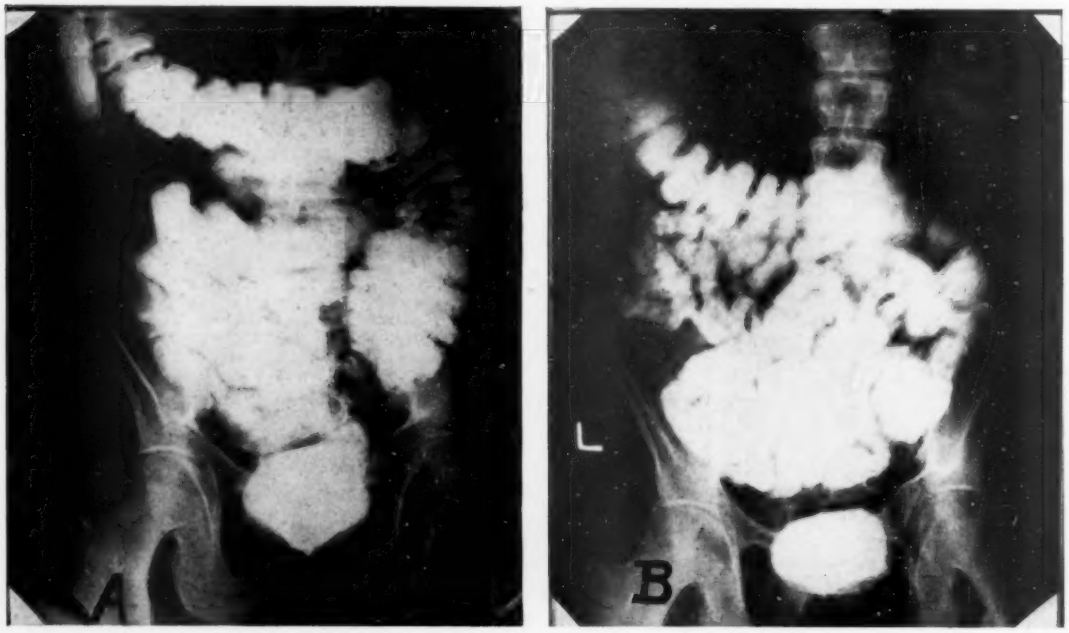

FIG. 2. *The effect of mecholyl. A.* The film before giving the drug shows the colon distinctly atonic. *B.* After the oral administration of 50 mg. of mecholyl the colon is markedly spastic. The patient suffered a moderately severe reaction which lasted about forty minutes.

Mecholyl is parasympathomimetic and causes hypertonicity with increased peristalsis. Its effects are visible in the entire gastrointestinal tract. It is a cholin derivative and chemically is acetyl-beta-methylcholin. The best results are obtained after subcutaneous injection, the average dosage being 20–30 mg. When given orally, the changes are inconstant and less satisfactory. The first effect, visible in five to ten minutes, is a heightening of tonus; this is soon followed by a marked increase in peristalsis, several deep, powerful waves being present simultaneously. In the colon, there is narrowing of the lumen, the haustrations being increased both in number and depth.[3] The effect lasts from thirty minutes to several hours.

With this drug, there may occur reactions of an unpleasant nature with profuse sweating, salivation, chilliness, headache, nausea, vomiting, and diarrhea; the blood pressure falls and there is a slowing of the pulse. These symptoms can be controlled by atropine. We do not believe that mecholyl at the present time is suitable for use by the roentgenologist in his routine work; for experimental or research purposes, however, it has a definite and important place.

In physostigmine, we have a drug which produces effects similar to those of mecholyl, but without the unpleasant side effects of the latter. We have used physostigmine in our clinic for nine years and have found it a very valuable addition to our arma-

mentarium. It causes first an increase of tonus with a contraction of the entire stomach; the margins of the gastric lumen become sharply delineated and more clearly outlined. Within five to ten minutes, there is an increase in peristaltic activity and several deep, vigorous waves are present. The opaque meal is forced into every portion of the stomach and through the pylorus and duodenum. Indurative or infiltrative lesions of the gastric wall may be visualized by the break in peristalsis at the site of the lesion; while defects due to spasm or extrinsic pressure cause no interference with the passage of the waves. Even in pylorospasm the force of the peristalsis induced by the drug may be sufficient to force the opaque meal through the sphincter and permit of visualization of the pylorus and duodenum. In an earlier paper,[1] this was mentioned as one of the indications for the use of the drug. However, by the use of benzedrine, which is to be discussed below, we have a more satisfactory agent to abolish pylorospasm and do not now feel that physostigmine is the drug of choice in this condition. In cases of obstruction of the pylorus by ulcers or neoplasms, the extent of the pathological process may in some instances be better demonstrated after the administration of physostigmine.

The effect on tonus is prolonged, frequently lasting an hour or more. The peristaltic changes, however, occur in only about 85 per cent of the cases and are usually present for only fifteen to thirty minutes. The peristaltic activity may also be intermittent; hence frequent, short roentgenoscopic observations are essential in order to fully observe the effects of the drug. Another great advantage of this agent is that it is effective when administered orally. The dosage for the average patient is 2.6 mg. (1/25 grain) by mouth. We prefer the sulphate or salicylate, and use the tablets. These may be given with the barium mixture or swallowed with a sip of water. The routine gastrointestinal studies need not be interfered with by the use of this drug. If injection methods are preferred, about one-half the oral dose can be used subcutaneously.

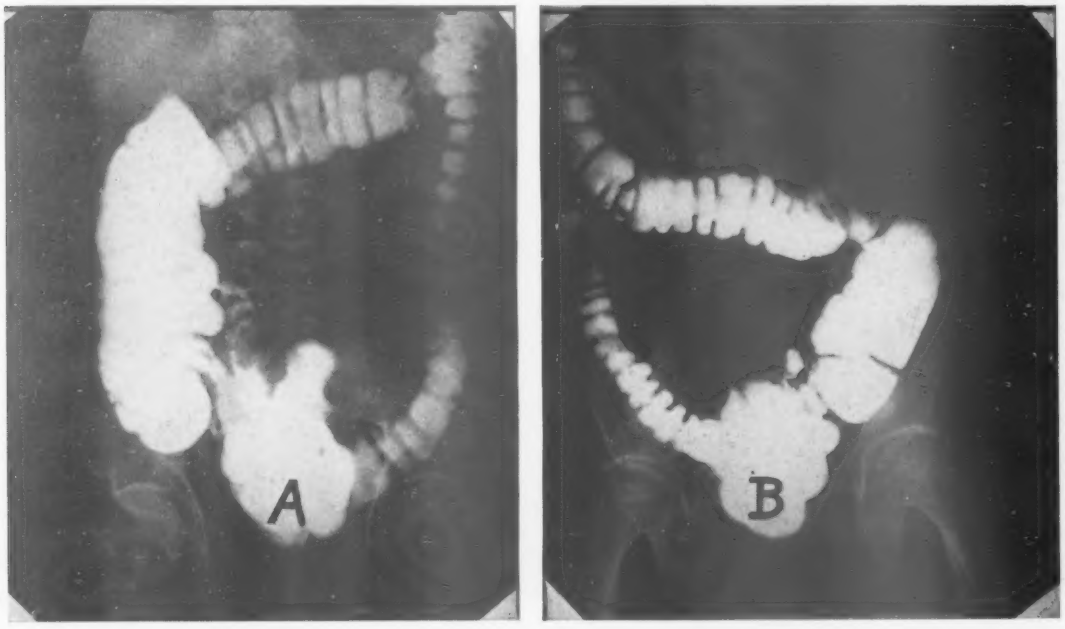

Fig. 3. *The effect of physostigmine. A.* The colon before giving the drug is atonic. *B.* After 1/20 grain of physostigmine salicylate orally, the colon is hypertonic with numerous deep, sharp haustrations.

Reactions rarely occur after the use of physostigmine. Malaise, nausea, and headache may be complained of, but these symptoms are usually mild and of short duration. More severe reactions with sweating, salivation, cramps, vomiting, and diarrhea are occasionally seen and can be controlled by the administration of 0.6 mg. (1/100 grain) of atropine sulphate orally or subcutaneously. The contraindications to the use of physostigmine are few in number and may be easily determined by inspection or complete questioning of the patient. The drug should not be administered in late pregnancy, severe heart disease, or iritis with redness and inflammation of the eye. In general, physostigmine may be used with safety in the doses recommended; the results are uniform and reactions are rare.

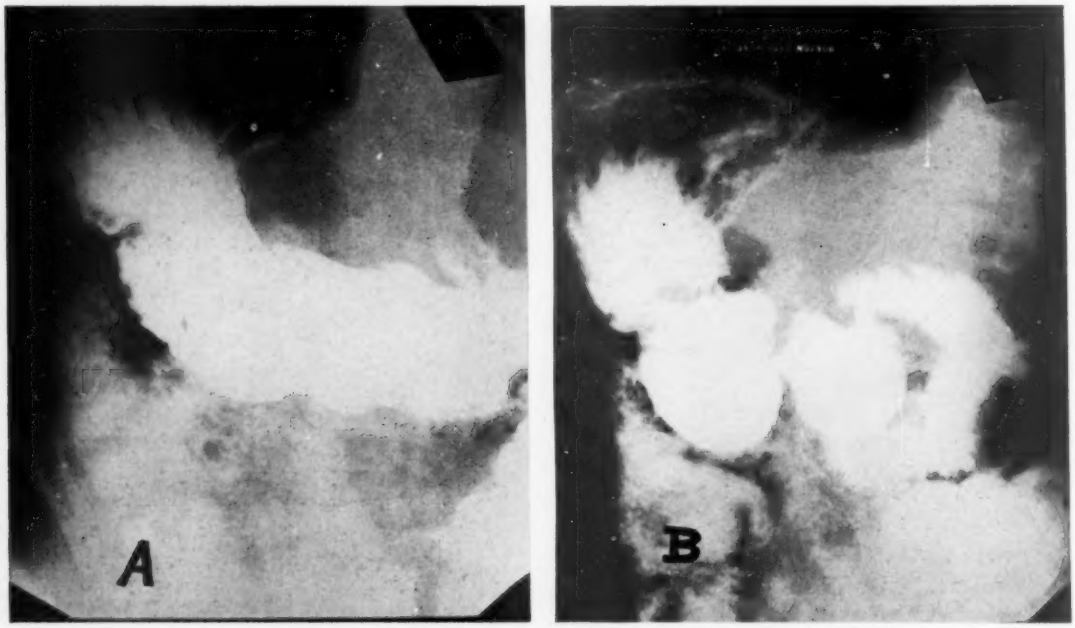

FIG. 4. *The effect of physostigmine. A.* The stomach before the drug was given is atonic, with sluggish peristalsis. The pylorus and duodenum are poorly filled. *B.* After the oral administration of 20 mg. of physostigmine salicylate orally, the stomach is hypertonic with vigorous peristalsis. The pylorus and entire duodenum are filled and an ulcer of the first portion of the duodenum is demonstrated.

DRUGS TO OVERCOME SPASM

Roentgenologists have long desired a satisfactory and effective method of abolishing spastic manifestations in the gastrointestinal tract. Spasticity is one of the most troublesome factors with which the roentgenologist has to deal. The deformities caused by spasm may very closely simulate organic lesions; spastic contractures may be superimposed on a pathological process and mask the true condition; or spasticity may be a reflex manifestation from extrinsic disease such as renal colic, plumbism, or tabes dorsalis and lead to a false diagnosis. Pressure over the stomach, reassurance, and the establishment of a pleasant mental state on the part of the patient during the roentgen examination may in some instances abolish the spasm; formerly if these measures were unavailing, as was frequently the case, re-examination at a later date was necessary. If the spasm had not disappeared in the interim, the roentgenologist had no other recourse and in many instances could not arrive at a definite conclusion. Atropine is recommended by many authors. Our experience definitely indicates that atropine is ineffec-

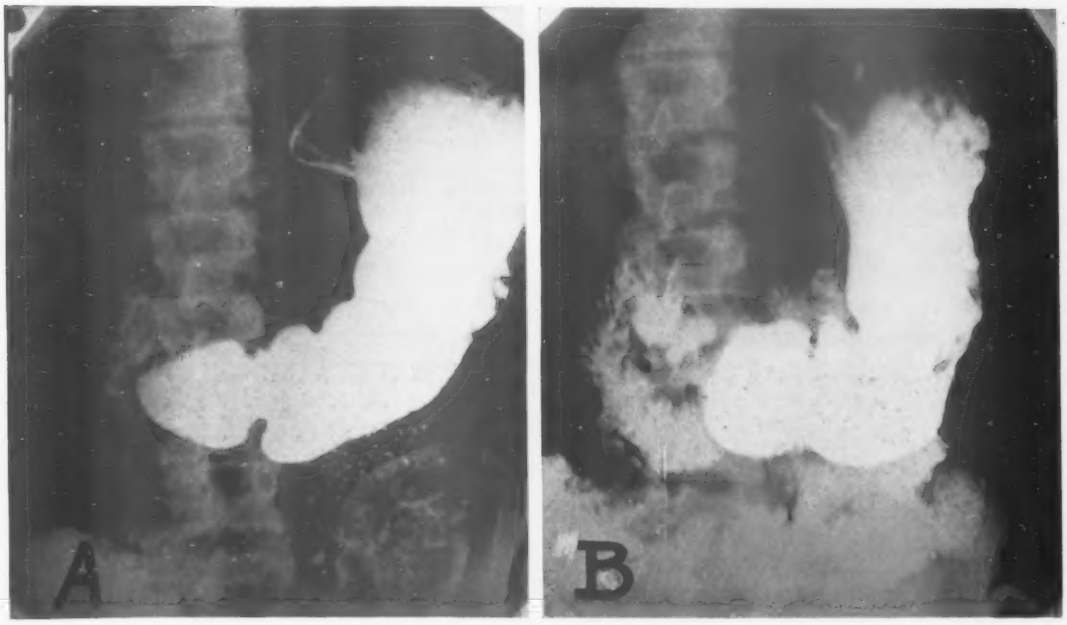

Fig. 5. *The effect of benzedrine sulphate. A.* Before the drug was given, the pylorus is markedly spastic and the duodenum only very slightly filled. *B.* After giving 30 mg. of benzedrine sulphate orally, the duodenal cap is well filled and shows the typical deformity of ulcer. The tonus is slightly diminished, but peristalsis is active under the influence of the drug.

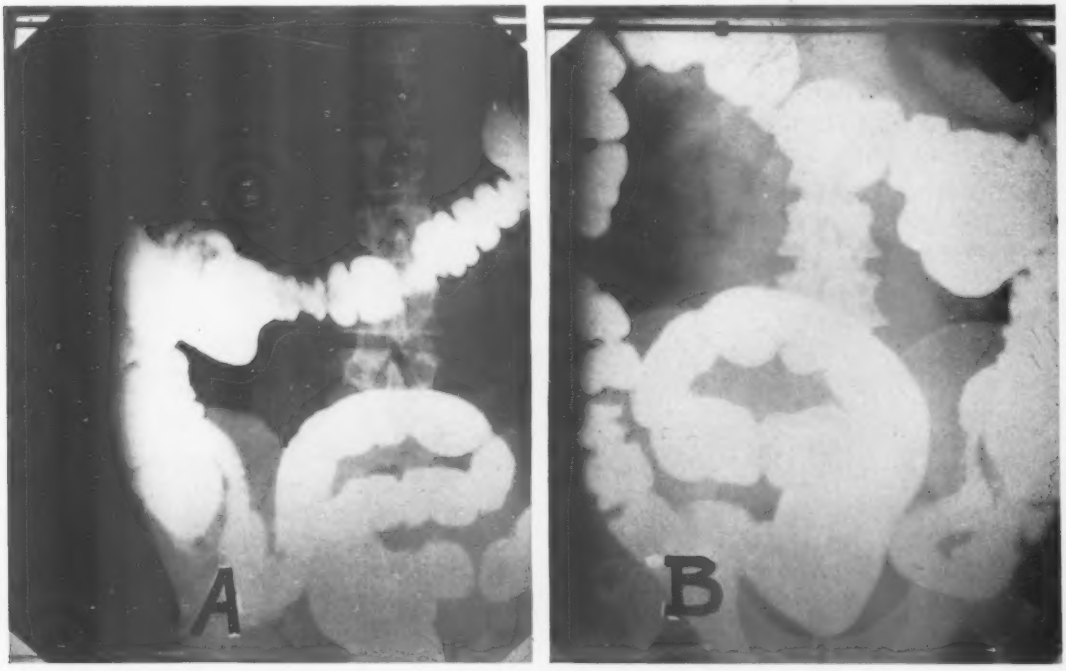

Fig. 6. *The effect of benzedrine sulphate. A.* The colon filled with opaque enema before the drug was given is spastic with many deep haustrations. *B.* After 30 mg. of benzedrine sulphate orally, the colon is atonic; the haustrations are markedly diminished in number and depth.

tive; in fact in some of our experiments it appeared that the spasm had actually been increased by this drug. Amyl nitrite relaxes spasm of the colon, but is useless in gastro- or pylorospasm; with this agent syncope and loss of sphincter control may occur, making it unsatisfactory for our purposes.

After many experiments, we found in benzedrine an agent which is effective in abolishing spasm of the gastrointestinal tract. Benzedrine is a synthetic derivative of ephedrine with the chemical formula $C_6 H_5 CH_2 CH NH_2 CH_3$. The sulphate of benzedrine is a stable compound in tablet or liquid form and may be given orally or by injection methods. This drug is sympathomimetic in character and its administration is followed by a relaxation of spasm of the stomach, pylorus, and intestines. More accurate study of the stomach and duodenum is possible after the disappearance of the spasticity as the stomach empties more readily; and small ulcer craters, especially about the pylorus and duodenum, are much more clearly visualized. The tonus of the stomach is lessened, but peristalsis is diminished only slightly by benzedrine; this is very important to the roentgenologist as peristaltic activity is of great aid in roentgen studies of the stomach. The colon becomes widened, the haustrations diminish in number and depth, and spastic deformities of the bowel disappear after the administration of the drug. In cases of spasticity of the colon, the patient is enabled to retain the opaque enema with much less discomfort if benzedrine has been given prior to the examination.

The optimum dosage for purposes of roentgen study is 20–30 mg. of benzedrine sulphate orally. The effect begins in five to ten minutes and lasts about one-half hour. If the results are unsatisfactory, we do not recommend further doses at the time, but rather a re-examination with a slightly larger dose at a subsequent date. Most patients experience a distinct feeling of well-being after the administration of benzedrine. The drug is apt to interfere with sleep if taken in the late afternoon, hence we prefer to use it in the forenoon. A moderate rise in blood pressure occurs with the above dosage. In a few instances, we have noted chilliness, flushing, malaise, and headache; in general, however, we feel that the drug may be administered safely in the doses recommended.

On theoretical grounds, it was felt that atropine and benzedrine in combination would work to greater effect than either drug alone, with a heightening of the effect so that smaller doses could be used and the possibility of reactions reduced or altogether eliminated. Experiments with various combinations of these agents did not bear out this expectation. The use of atropine and benzedrine together was distinctly less effective than benzedrine alone.

SUMMARY AND CONCLUSIONS

Drugs are a valuable aid to the roentgenologist in his studies of the gastrointestinal tract.

By the use of the proper drug, the roentgen examination may be facilitated and greater accuracy of diagnosis attained.

Mecholyl and physostigmine are used to increase tonus and peristalsis; these drugs are valuable in cases with atonicity and sluggish or absent peristalsis.

Benzedrine is useful in abolishing spastic manifestations in the stomach and intestines.

The indications, dosages, and methods of administration are described.

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Vol. 36, No. 6

GASTRIC CANCER

A CLINICAL ROENTGEN STUDY WITH PARTICULAR REFERENCE TO EARLY DIAGNOSIS

By D. S. BEILIN, M.D.
Radiologist, Augustana Hospital
CHICAGO, ILLINOIS

CANCER of the stomach is responsible for about one-third of all the deaths annually from cancer in the male. It is estimated that 38,000 persons die each year in the United States from cancer of the stomach. It is a lamentable fact that by the time the case of cancer of the stomach comes to the clinician, approximately 50 per cent have reached a stage in which not even an exploratory operation is indicated. In the other 50 per cent, in which an exploration is warranted, the growth can be removed in only about one-half of such cases. Thus it will be seen that only 25 per cent of the cases of cancer of the stomach are operated on at a time when an attempt at a cure can be made.

This appalling situation is due to many reasons: procrastination on the part of the patient who has "indigestion"; failure to make an early diagnosis; the generally accepted criteria for the diagnosis of gastric cancer are the late manifestations of the disease; the early syndrome of gastric cancer will have to be popularized and the public made "stomach conscious"; lack of knowledge of the etiology of carcinoma; the absence of any specific serologic tests for its presence; the prevailing attitude of many physicians and of laymen toward the disease, namely, when a diagnosis of cancer of the stomach is made, the condition is considered incurable and nothing is done.

Among the 1,000 consecutive examinations of the stomach in this study there were 71 cancers, or 7.1 per cent. The youngest age in this study was twenty-six years. Extensive carcinomas of the stomach may occur at a much earlier age, as exemplified by a case reported by Levene and Wheatley, who cite a case of a very extensive carcinoma of the stomach in a girl, aged nineteen. It is interesting to note that for five months prior to admission to the hospital the patient had been under the care of her physician for the treatment of a nervous breakdown.

This study revealed that the highest incidence of cancer of the stomach occurred in the fifth and sixth decades of life, with the average age being fifty-eight years, and the disease is almost twice as common in males as in females.

Although the etiology of carcinoma of the stomach is unknown, Ewing states it is very likely that gastric cancer begins as a localized overgrowth, affecting primarily previously normal cells which show atypical overnutrition and overgrowth, and infection, erosion, and ulceration may supervene very early. Other investigators emphasize the incidence of carcinoma in chronic ulcerating lesions of the stomach. Haudek, in reviewing his experience in the roentgen diagnosis of gastric lesions, recognized the difficulty in distinguishing between the benign and malignant lesions at the prepyloric region. The prepyloric region, he stated, is the most frequent site of cancer; about 80 per cent of the carcinomas start there. Holmes and Hampton believe it is fair to state that any chronic indurated ulcerating lesion occurring at the pyloric antrum within 1 inch of the pylorus and without involving the pylorus should be considered malignant until proved to be otherwise, and that proof of the absence of malignancy in such lesions is obtained only by serial section and careful microscopic examination. This study revealed that 78 per cent of the carcinomas of the stomach occurred at the pylorus and antrum, whereas 12.3 per cent occurred at the middle third and only 8.2 per cent occurred

at the upper third of the stomach.

In a study made by the Cancer Commission of Harvard University, among 1,059 autopsy cases of malignant disease selected from the material of the Huntington Memorial Hospital, the New England Deaconess Hospital, the Pondville State Hospital, and the House of the Good Samaritan, 69 cases of malignant disease of the stomach were encountered. Over half of the cancers were classified as adenocarcinomas; the carcinoma simplex or undifferentiated carcinoma was the next most frequent type, with 19 cases. Colloid carcinoma was encountered 7 times and lymphosarcoma and fibrosarcoma once each. The criteria which they used in subdividing carcinoma on histologic grounds were relatively simple; those tumors which showed well-formed alveoli in at least 25 per cent of the regions examined were classified as adenocarcinoma. The other large group, the carcinoma simplex or undifferentiated carcinoma, tends to be markedly anaplastic and less than 25 per cent of the tumor shows alveolar arrangement. These tumors again may be either scirrhous or medullary. The infiltrating cancer of the signet-ring type, although considered by some as a subvariety of the colloid carcinoma, they believe to be more properly placed here. The colloid or gelatinous carcinomas are those in which there is a considerable degree of secretory activity, in many places so marked as to show only mucinous secretion or small clusters of tumor cells separated from their stroma afloat in pools of mucus. Grossly, these tumors are bulky, infiltrating, and rather soft, with a peculiar watery translucence on section. The malignant adenoma is similar to the form encountered in the large intestines. It is a polypoid tumor, infiltrating late with anaplastic epithelium, usually only one cell thick, lining numerous irregular alveoli.

Their observations on metastases of cancer of the stomach are of prime importance. The relatively restricted distribution of metastases is striking. This undoubtedly is due in part to the short duration of the disease and the location of the primary tumor being such as to cause death rather than death being brought about by secondary changes in other organs. Aside from the regional lymph nodes, most metastases lodge in the liver and on the peritoneal surfaces. After these, the distant nodes, the pancreas, and the lungs are involved in order of frequency. Less than 10 per cent of the cases metastasize to the lungs. Only 9 instances of metastases above the diaphragm were detected. There were only 18 sites of metastases. There were 4 metastases to bone, 2 from adenocarcinoma and 2 from carcinoma simplex. Metastases to bone with cancer of the stomach are more frequent than is usually supposed. These metastases were all of the osteoclastic type and probably were hematogenous. Omitting lymph nodes, there were only 22 instances of metastases to sites which were more or less widely scattered, in contrast to 61 to nearby structures. No true Krukenberg tumor was encountered, although there were 3 metastases to the ovary.

The relative restriction of metastases is of importance from a clinical standpoint. If metastases are not found in adjacent lymph nodes and in the liver at the time of operation, the chance of more distant involvement having already occurred is relatively slight.

A knowledge of the gross morphology of gastric cancer is of paramount importance. Early attempts to fit roentgenologic findings into one of the many pathological classifications were made by Cole. Cole's recent contributions on the correlation of the roentgenologic findings with the morphology of the lesions as observed in the gross pathological specimen is of practical scientific interest. His work emphasizes the importance of, as well as the information gained by the radiologist correlating from his attendance at operations and autopsies the surgical and pathological findings with his own roentgenologic findings.

Unfortunately, cancer of the stomach

presents no typical early syndrome. When patients present the classical picture of gastric malignancy, as has been so often described, with marked loss of weight, emaciation, pain, vomiting, palpable tumor mass, etc., the disease is advanced. Lahey, Swinton and Peelen discuss the early symptoms of cancer. Their study is based on a series of 195 cases during the past seven years at the Lahey Clinic. The earliest symptoms of cancer were indigestion 70 per cent, anorexia 42 per cent, pain 30 per cent, weight loss 25 per cent, vomiting 28 per cent, dysphagia 4 per cent, weakness 13 per cent, hemorrhage 4 per cent, constipation 7 per cent, diarrhea 7 per cent, mass 1.5 per cent. The average weight loss in 163 cases was 25.7 pounds. The duration of symptoms in their patients, who at operation presented an operable lesion, was 8.1 months; in the inoperable group it was 8.5 months.

An analysis of the early clinical findings of cancer of the stomach in my series (symptoms under three months in duration) revealed indigestion 76.9 per cent, pain 30.7 per cent, nausea 92.3 per cent, vomiting 84.6 per cent, vomiting blood 23 per cent, relief by food, soda, or medicine 0.76 per cent, weakness 69.2 per cent, average weight loss 16.7 pounds. It can readily be seen that the early symptomatology of gastric cancer varies in different individuals. However, if one indelibly bears in mind that if there are symptoms in an individual over forty years of age, who complains of indigestion, as well as loss of appetite, nausea, vomiting, abdominal pain, fatigue, loss of weight without obvious cause, unexplained anemia, or any group of the above, one should regard this individual as having carcinoma of the stomach until proved otherwise. It should be popularized to the general profession and laity that the early clinical signs of cancer of the stomach are often so vague and apparently so insignificant, and that usually the earliest symptom is so-called "indigestion"; and in order to make a diagnosis of a beginning cancer, thorough and competent clinical and roentgenologic examinations must be made at the time that the individual first presents himself, for the discovery of a carcinoma at that time will remarkably increase the percentage of cures.

During the past few years continued interest has been manifested by numerous investigators such as Links, Epstein, Tisserandet, Weber and Schüle, Roffo, Gandolfo, and Freund, on the biologic and serologic methods for the early diagnosis of cancer. Although marked advancement has been made, the fact remains that at the present time there is no generally accepted serologic or biologic test for cancer of the stomach.

The following investigators have presented contributions on the early diagnosis of gastric cancer: Kirklin, Cross, Rigler, Percy and Beilin, Stewart and Illick, Vespignani, Cole, and others. Many clinicians have gone to great length to emphasize the limitations of the roentgen examination in the diagnosis of cancer. This is true in a very small percentage of the cases, for the tumor may be so located or its pathological characteristics so slight that on a cursory examination, it may not be demonstrable. This is particularly true of early cancer at the cardiac portion of the stomach which may elude discovery unless this region is inspected very carefully. It should always be remembered that if, in a single examination, an early carcinoma is not revealed when suggested clinically, and if no other pathology is elicited to account for the symptomatology, repeated examinations at short intervals of time can always be done, for not infrequently a second examination may denote very slight changes which were not observed at the previous examination which might indicate very early pathological changes due to carcinoma.

There are several varieties of early cancer: (1) early prepyloric cancers; (2) small ulcerating carcinomas; (3) small malignant tumors or infiltrations with only slight or imperceptible ulceration; (4) malignant ulcers.

(1) Early prepyloric cancers are sometimes perplexing for the narrowing of the antrum that they may produce may be imitated by that resulting from benign ulcer with spasm, hypertrophy of the rugae, hypertrophy of the pyloric muscle, and syphilis. Usually a careful roentgenoscopic examination in all positions as well as roentgenograms at all angles will show some signs which are indicative of carcinoma, namely a slight, irregular, marginal defect, and on manual pressure the rugae of the stomach are either smoothed out or are entirely effaced.

In benign ulcer with spasm, the niche is small, the border at the base of the niche is smooth, and as a rule there is normal arrangement of the adjoining rugae. There usually is localized tenderness on palpation over the site of the niche. If the ulcer is unduly large with a diameter of more than 2.5 cm., it will usually prove to be malignant. Associated with this large niche, there is usually some irregularity of the border or base of the niche with effacement of the normal arrangement of the adjoining rugae with absence of gastrospasm and usually absence of localized tenderness.

Hypertrophic rugae can usually be identified by their pronounced parallel markings, whereas pyloric hypertrophy usually causes a slight, rounded invagination of the bulbar base, and is also marked by a crevice at the middle of the greater curvature of the narrowed canal; these signs are wanting in carcinoma.

Syphilis tends to convert the affected gastric segment into a narrow tube with a relatively smooth lumen of uniform caliber, and the gastric wall is almost never palpable. Likewise the extent of deformity is out of proportion to the clinical condition of the patient. Other signs of lues may be present and the Wassermann and Kahn tests are usually positive.

(2) The small ulcerating carcinoma may resemble simple ulcer with the exception that in malignant lesions tumefaction persists in a sufficient degree to form a slightly elevated border about the ulcerous excavation. If the malignancy is on the lesser curvature, the ridge appears under pressure as a semicircular, clear strip separating the shadow of the barium-filled crater from that of the stomach. If the lesion is on the posterior wall, the ridge is seen under pressure as a transradiant halo about the dense crater. The crater does not project beyond the normal confines of the gastric lumen. There is slight tenderness on palpation and gastrospasm is usually absent. The meniscus-complex is practically pathognomonic of ulcerating cancer and was described years ago by Carman.

(3) Small malignant tumors or infiltrations with only slight or imperceptible ulceration are occasionally seen. Because they usually have pedicles they are often mistaken for benign growths. When these are discovered, although they may have a benign appearance, they should be reported as malignant. Early infiltrating scirrhous cancer involving a small area may be exceedingly hard to elicit, for it seldom produces an obvious marginal defect. However, serial roentgenography will usually reveal that the curvature is abnormally smooth and peristalsis absent, and not infrequently the normal angular incisura is lacking. A more convincing and reliable sign of early scirrhous cancer, as emphasized by Kirklin, is the granular, internal relief which it produces. Thoroughly planned examinations must be done in order to detect very early malignancy at the cardia. One may see retarded flow of barium from the esophagus, division of the barium stream by a small tumor, irregularity or deformity of the normally smooth and symmetrical gas bubble, and on careful roentgenoscopic examination with palpation, after the patient has swallowed only one or two mouthfuls of barium, one may see a large fleck ulcer or irregularity in the normal pattern.

(4) Malignant ulcer is a term conveniently reserved for ulcers that, in contrast with ulcerating carcinoma, present neither macroscopic nor roentgenologic evidence of tumefaction, yet on microscopic examina-

tion are found to contain cancer cells. It has long been accepted that when the diameter of an ulcer crater is 2.5 cm. or more, the ulcer is probably malignant. When the ulcer is smaller than this, other indications of malignancy have to be considered. Among these are irregularity of the niche, obliteration of the neighboring rugae, absence of gastrospasm and lack of tenderness on localized pressure over the niche. Ulcers on the greater curvature are usually malignant; ulcers on the posterior wall or at the prepyloric area are more likely to be malignant than those on or near the mid-section of the lesser curvature. On the other hand, most niche ulcers are benign; usually the niche is dense, regular in form, lies in the midst of converging rugae, is sensitive to pressure, and spastic accompaniments are common. The points of distinction between cancer and benign lesions have been emphasized because accuracy in their differential diagnosis is of paramount importance. In the interest of the patient, the roentgenologist should be rather skeptical as to the benignancy of any tumor or ulcer of the stomach. Unless the roentgenologist can affirm confidently that the lesion is benign, he should not return this diagnosis without qualification.

CONCLUSIONS

1. It is very likely that gastric cancer begins as a localized overgrowth, affecting primarily previously normal cells which show atypical overnutrition and overgrowth, and infection, erosion, and ulceration may supervene very early.

2. There is ample evidence to show that occasionally cancer may develop from an ulcer. No conclusive statistics are available as undoubtedly some of these cases which have been said to be malignancy developed on ulcer are small adenocarcinomas which ulcerate at an early stage, and the tumor may be so completely excavated by digestion and infection that no trace of the original carcinoma can be observed.

3. A knowledge of the gross morphology of gastric cancer is of paramount importance in the early diagnosis of cancer.

4. The general profession and laity should be made aware of the fact that the clinical signs of cancer of the stomach are often vague and apparently insignificant, and that usually the earliest symptom is so-called "indigestion"; and in order to make a diagnosis of a beginning cancer, thorough and competent clinical and roentgenologic examinations must be made at the time that the individual first presents himself, for the discovery of a carcinoma at that time will decidedly increase the percentage of cures.

5. The roentgenologic diagnostic aspects of early gastric cancer have been presented in detail as well as other conditions which must be differentiated from early carcinoma. It is obvious that the roentgenologic examination is the most valuable procedure in the diagnosis of early gastric cancer.

6. Serologic, biologic, and other laboratory procedures are of no conclusive value in the diagnosis of early gastric carcinoma.

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LYMPHOBLASTOMA OF THE GASTRO-INTESTINAL TRACT*

By WILLIAM C. MARTIN, M.D.
LOUISVILLE, KENTUCKY

THIS paper deals with the diagnosis of lymphoblastoma as it involves the gastrointestinal tract primarily or secondarily. The term "lymphoblastoma" as used at the Massachusetts General Hospital is based upon Mallory's classification and includes Hodgkin's lymphogranuloma, lymphosarcoma, lymphoma, leukemia and aleukemia. Since different types of lymphoblastoma show the same response to deep roentgen therapy and, when present in the gastrointestinal tract, show similar changes when examined with the barium meal, we have found it convenient for this study to group them under this general heading. There has been a tendency in recent years to group all these diseases under the generic term lymphoblastoma, adding a qualifying clinical classification. Thus, lymphatic leukemia becomes lymphoblastoma, leukemic; aleukemia lymphatic leukemia, lymphoblastoma aleukemicum; mycosis fungoides, lymphoblastoma cutis; Hodgkin's disease, lymphoblastoma (Hodgkin's type), and lymphosarcoma, lymphoblastoma (infiltrating type).

In reviewing the literature we were surprised to find that the Hodgkin's type of this disease was reported much more frequently than the other forms. The literature previous to the year 1913 contained no cases of gastrointestinal Hodgkin's disease, and this fact was used clinically in cases of superficial glandular enlargement as favoring the diagnosis of leukemia. In 1913, Schlagenhaufer reported the first proved case of gastrointestinal Hodgkin's disease. Since then nearly 100 cases of Hodgkin's type of lymphoblastoma of the gastrointestinal tract with only an occasional case of the other types of lymphoblastoma have been reported. Most of these cases can be found in the excellent article by Coronini. Wells and Maver in 1904, gave a historical study of gastrointestinal leukemia.

In addition to a summary of the reported cases, this paper presents 19 cases of proved lymphoblastoma involving the gastrointestinal tract studied at this Hospital since 1925. The cases up to that time were reported by Holmes, Camp and Dresser.

CASE REPORTS

CASE I (270861). T. H. W. Male, aged sixty-one. Date of admission, July, 1925; death at operation. Onset of symptoms, four months previously with diarrhea and loss of weight. Glands, spleen, liver and skin negative. Temperature normal. Red blood count, 4,400,000; white blood count, 10,200; hb, 60 per cent. Roentgen diagnosis was malignant obstruction at the pyloric end of the stomach. Preoperative diagnosis was stricture of the rectum and carcinoma of the stomach. Operative findings: tumor mass involving the antrum, pylorus and infiltrating beyond the pyloric valve to involve the duodenum. Biopsy section showed lymphoblastoma. No autopsy.

CASE II (279281). C. L. Male, aged forty. Date of admission, October, 1926; died in December, 1926. Onset of symptoms, May, 1926, with epigastric pain and drenching night sweats. Superficial glandular enlargement. Spleen and liver palpable. Skin negative. Temperature 100–103° F. Red blood count, 4,300,000; white blood count, 3,050; hb, 60 per cent. Stools negative for blood. Chest and gastrointestinal tract were negative by roentgen examination. No operation. Biopsy: lymphoblastoma. Autopsy showed lymphoblastoma involving the spleen, liver, mesenteric lymph nodes and two small nodules on the terminal ileum.

CASE III (291011). A. P. Male, aged thirty-two. Date of admission, January, 1927; patient discharged from hospital and did not return for follow up observation. Date of onset, Novem-

* From the Department of Roentgenology, Massachusetts General Hospital, Boston, Massachusetts.

ber, 1926, with colicky abdominal pain not related to food. Skin, glands, spleen, and temperature not remarkable. Red blood count, 5,000,000; white blood count, 28,000; hb, 100 per cent. No roentgen examination made. Preoperative diagnosis: chronic intestinal obstruction. Operative findings: small tumor on terminal ileum 12 inches from the cecum with enlarged glands. Twelve days later, abdomen reopened and diffuse purulent peritonitis found but anastomosis intact. Two months later, a residual abdominal abscess drained. Biopsy of tumor: malignant lymphoma.

Case iv (295907). T. P. P. Male, aged sixty-two. Date of admission, December, 1928; died at operation. Onset of symptoms seven months previously associated with tarry stools and hematemesis. Jaundice one month previous to admission. Posterior gastroenterostomy, 1912. Slight superficial glandular enlargement, spleen negative, liver palpable. Skin and temperature not remarkable. Red blood count, 4,700,000; white blood count, 16,000; hb, 75 per cent. No roentgen examination made. Preoperative diagnosis: cancer of the stomach. Operative diagnosis and biopsy: lymphoblastoma (lymphoma) of the stomach. Autopsy showed lymphoblastoma involving the stomach, intestine, liver, spleen, and abdominal glands. Generalized peritonitis.

Case v (296620). L. S. Male, aged fifty-two. Date of admission, January, 1929; patient died in hospital four months later. Onset four months before admission, continuous left upper quadrant pain. Hiccoughs for five years. Skin, glands, and spleen negative. Temperature 100–101° F. Roentgen examination of the chest showed a high fixed left diaphragm suggesting that the lesion was below the diaphragm. Cystoscopic examination was recommended. Retrograde filling of left kidney showed it to be displaced downward by a mass. Barium enema was negative. Stomach was not examined. Preoperative diagnosis: subphrenic abscess. Operative findings: subphrenic abscess and pancreatitis. March, 1929, removal of pus in spleen. April, 1929, left rib resection for drainage. May, 1929, patient died. Biopsy report of spleen: septic infarct. Autopsy showed lymphoblastoma of stomach, retroperitoneal glands and spleen. Marked infiltration of the left diaphragm with lymphoblastoma. There was an ulcer of the fundus of the stomach 3 cm. in diameter with marked thickening and distortion of the rugae. Acute pleuritis; 4,000 c.c. of ascitic fluid.

Case vi (287019). G. M. Male, aged eighty-one. Date of admission, October, 1929; died, November, 1929. Onset of symptoms three years before with enlarged cervical glands; three weeks previous to admission, marked pallor and weakness. Superficial glandular enlargement. Spleen and liver grossly palpable. Temperature 100° F. Rectal mass. Red blood count, 3,720,000; white blood count, 150,000; hb, 55 per cent. (Lymphatic type of cells.) Non-protein nitrogen, 90. Roentgen examination of the chest was negative. Patient received 100 ma-min. deep roentgen therapy to the spleen. Died on November 2, 1929. Autopsy showed malignant lymphoma—lymphatic leukemia. Stomach showed marked thickening and distortion of the rugae with slightly raised areas 1 to 2 mm. in diameter. Duodenum and jejunum showed prominent patches of lymphoid tissue. Ileum showed marked hypertrophy of Peyer's patches with occasional ulcerations. Terminal ileum and ileocecal valve were markedly thickened and there was herniation of the terminal ileum into the cecum. Cecum showed prominent rugae studded with small raised patches. Bladder and rectum infiltrated with tumor mass. Spleen enlarged.

Case vii (296964). J. O. B. Male, aged fifty-five. Date of admission, February, 1929; died December 15, 1932. Onset of symptoms in January, 1928, with enlarged inguinal glands. Five months previous to admission there was grinding epigastric pain which was relieved by food and soda. Positive test for diabetes. Skin showed pigmentation. Spleen palpable. Generalized glandular enlargement. Temperature normal. Red blood count, 4,950,000; white blood count, 7,500; hb, 80 per cent. Stools showed positive guaiac. Roentgen examination showed a filling defect 1.5 cm. in diameter involving the pylorus and antrum of the stomach associated with a deformity of the edges of the first and second portions of the duodenum (extrinsic duodenal involvement). The rugae showed moderate deformity and thickening. Biopsy of superficial glands showed lymphoblastoma, Hodgkin's type. Patient was treated from January, 1928, until December 15, 1932, receiving suberythema doses in large fields to the anterior and posterior abdomen given in

daily doses of 200 r each. By December, 1932, pyloric obstruction had become so complete that a posterior gastroenterostomy was attempted from which the patient did not recover. Autopsy showed generalized lymphoblastoma with a small hard nut-sized tumor mass at the pylorus, marked thickening and distortion of the gastric rugae, large duodenal ulcer, tumor mass in the head of the pancreas, and ampulla of Vater, marked involvement of Peyer's patches with tumor masses and a large mass involving the rectum and prostate.

Case VIII (305682). C. B. Male, aged thirty-seven. Date of admission, March, 1930; died in April, 1930. Onset of symptoms in 1929 with generalized glandular enlargement and weakness. Patient showed superficial glandular enlargement. Palpable spleen and liver. Temperature 100–101° F. Roentgen examination of the chest was more suggestive of tuberculosis than of lymphoblastoma. No examination was made of the gastrointestinal tract. Patient received 400 ma-min. to the spleen and died at the completion of the treatments. Autopsy showed miliary tuberculosis and caseous pneumonia; tuberculous enteritis and adenitis, lymphoblastoma (Hodgkin's type) involving the intestines and the glands of the mesentery and mediastinum. The lymphoblastomatous ulcers occurred side by side with the tuberculous ulcers. Red blood count, 3,200,000; white blood count, 3,200; hb, 30 per cent.

Case IX (B.M. 1126). E. T. G. Female, aged sixty-one. Date of admission, September, 1930; patient died January, 1931; no autopsy. Onset of symptoms, vomiting, diarrhea and faintness for three weeks. Skin, spleen, temperature not remarkable. Moderate cervical glandular enlargement. Red blood count, 3,800,000; white blood count, 7,600; hb, 65 per cent. Stools negative by guaiac. Roentgen findings in October, 1925, showed a tumor involving the ascending colon which was resected. Another examination by barium enema in 1930 showed moderate deformity of the transverse colon but no evidence of obstruction. Examination of the stomach was not requested and was not done. Preoperative diagnosis: recurrent cancer of colon. Operative findings: tumor mass involving the stomach, duodenum and remainder of the transverse colon. Operative diagnosis: grapefruit-sized tumor involving the walls of the transverse colon, duodenum, and stomach. Section of the tumor showed lymphoblastoma. Patient received 300 ma-min. to the posterior abdomen before she was discharged from the hospital.

Case X (B.M. 2615). E. H. P. Female, aged sixty-one. Date of admission, March, 1931. Patient living and well; showed no recurrence of symptoms when last seen in January, 1934. Onset of symptoms, October, 1930, with fatigue, increasing constipation, and a mass in the abdomen above the umbilicus. Stools black but not tarry. Skin yellow. Glands and spleen not palpable. Temperature, 100° F. Red blood count, 4,880,000; white blood count, 10,150; hb, 65 per cent. Roentgen findings: displacement of the transverse colon downward and to the left by an extrinsic mass. Examination of stomach not requested and not made. Preoperative diagnosis: mesenteric cyst. Operative findings: ulcerating tumor mass, 12×12 cm., involving the walls of the stomach, duodenum, and transverse colon; a tumor 5×5 cm. in the gastrocolic ligament and several smaller tumors in the mesentery. Surgical treatment: subtotal gastrectomy and resection of the involved colon. Biopsy report: lymphoblastoma. Patient was given a suberythema dose of deep roentgen therapy following the operation and this was repeated three months later.

Case XI (B.M. 5089). E. W. Male, aged forty-three. Date of admission, December, 1931. Patient last seen in April, 1932. He was working and gaining in weight, but still had some epigastric distress. Date of onset, April, 1931, with colicky epigastric pain, paroxysmal in character and relieved by milk and soda. Skin, glands, spleen and temperature not remarkable. Stools showed positive guaiac tests. Red blood count, 4,940,000; white blood count 6,800; hb, 75 per cent. Roentgen findings: large ulcerating tumor of the posterior wall and lesser curvature of the middle third of the stomach. Preoperative diagnosis: cancer. Surgical treatment: subtotal gastrectomy. Biopsy report: gastric tumor 6 cm. in diameter with marked enlargement and distortion of the gastric rugae; lymphoblastoma. Deep roentgen therapy started two weeks after operation and patient received 66 r through a 20×20 cm. field to the anterior and posterior abdomen.

Case XII (317894). L. G. Female, aged seventeen. Admitted December, 1931, and

died May, 1932. Sudden onset with constipation, anemia and abdominal mass that disappeared with bowel movement. Glands, skin, spleen and liver not remarkable. Temperature 99.4° F. Red blood count, 3,900,000; white blood count, 9,300; hb, 60 per cent. Stools showed positive guaiac tests. Urine positive for sugar. Barium enema showed enlarged sigmoid and stasis around the terminal ileum. Chest negative. Exploratory operation showed large sigmoid with grossly thickened walls and sanguineous peritoneal fluid. Large mass of glands in mesentery of the ileum. Retroperitoneal glands also enlarged. Biopsy report: lymphoblastoma. In February, 1932, patient received 600 r each to the front and back of the abdomen. Patient died in May, 1932. Autopsy showed glandular involvement of the chest and abdomen, cholangitis, cholelithiasis, gross thickening of the wall of the entire small bowel and of that of the sigmoid by lymphoblastoma. Numerous peritoneal nodules, and numerous 2×2 cm. ulcers of the entire small bowel.

Case xiii (316830). S. F. Female, aged sixty-one. Date of admission October, 1931. Patient had been treated with deep roentgen therapy, 600 r to the front and back of the pelvis for two and a half years at four month intervals. These treatments had given complete relief to obstruction signs and symptoms. Onset of symptoms February, 1930, with bloody stools and diarrhea alternating with constipation. Pain over the tip of the sacrum. No loss of weight. Glands, spleen, liver, skin and temperature not remarkable. Red blood count, 4,580,000; white blood count, 6,800; hb, 80 per cent. Proctoscopic examination showed "cartilaginous" thickenings of the rectal valves associated with numerous ulcers which did not resemble cancer. Roentgen examination of the stomach showed no enlargement of the gastric rugae but a definite duodenal ulcer. Biopsy: lymphoblastoma. No surgical treatment. With deep roentgen therapy the recurrent signs of obstruction have been entirely relieved for periods lasting from three to four months.

Case xiv (B.M. 5514). Dr. W. Male, aged fifty-four. Admitted February, 1932; died August, 1933. Onset of symptoms was insidious. Five years ago a gastrointestinal examination revealed both a gastric and duodenal ulcer, while the patient was being treated for diabetes. One month previous to admission to the hospital he noted slight general glandular enlargement. Weakness had been noted by the patient for one year. Examination showed general glandular enlargement, palpable liver and spleen. Normal temperature. White blood count, 8,300; red blood count, 4,670,000; hb, 75 per cent. Re-examination of the gastrointestinal tract at this hospital revealed the displacement of the fundus by the enlarged liver and spleen, some increase of the gastric rugae, deformity of the pyloric valve and duodenal loop by extrinsic pressure in the region of the pancreas and the duodenal ulcer. Biopsy of a gland showed lymphoblastoma. After the patient received deep roentgen therapy, the fundus of the stomach returned to its normal position and the extrinsic pressure defects on the pylorus and duodenal loop disappeared.

Case xv (321262). T. C. Male, aged sixty. Admitted May, 1932; died June, 1932. Onset of symptoms three months previous to admission. Chief complaint was indigestion and swelling of the abdomen associated with epigastric and precordial pain. The first roentgen examination of the gastrointestinal tract showed a gastric ulcer. At the second examination, after ulcer diet without improvement, a diagnosis of gastric cancer was made. The patient was admitted to the hospital with the diagnosis of inoperable cancer. When first admitted to the Roentgen Department, he showed multiple lesions of lymphoblastoma. A biopsy was requested which confirmed the roentgenologic diagnosis of lymphoblastoma.

Case xvi (325939). S. T. G. Female, aged fifty-three. Admitted December, 1932. Onset of symptoms one year before with epigastric pain coming on one hour after meals relieved by soda and milk. Later the pain radiated to the shoulder and recently the pain was entirely localized to the left epigastrium and not relieved by soda and diet. Lost 20 lb. in weight. Red blood count, 4,500,000; white blood count, 7,600; hb, 60 per cent. Guaiac test positive only once. Liver, spleen, and glands not remarkable. Normal temperature. The gastrointestinal examination showed a large ulcerating lesion on the greater curvature of the stomach associated with prominent gastric rugae. At operation, the lower 20 cm. of the stomach was resected and biopsy showed lymphoblastoma. The case was not followed.

Case xvii (326809). B. C. Mc. Female, aged sixty-four. Admitted January, 1933. Eight weeks before admission sudden onset of diarrhea and lower abdominal cramps. No blood or mucus. Attack followed by bloating and sudden relief by the passage of a large amount of gas. Guaiac test positive only once. Barium enema was negative. Rectal examination showed metastatic glands in the cul-de-sac. Biopsy of glands showed lymphoblastoma. Relief by deep roentgen therapy.

Case xviii (314944). N. I. Male, aged forty-six. Date of first admission, 1931. Symptoms of weakness, joint pains and alternate periods of constipation and diarrhea. In the interval between the two admissions he had night sweats, burning epigastric pains and weakness. No nausea or vomiting. Patient was sent to Roentgen Department for examination with a barium enema which showed spastic colitis. In 1933, the stomach was examined for the first time and showed a large saddle ulcer occupying the middle third of the lesser curvature. This was associated with gross deformity of the gastric mucosa. Chest was negative. Surgical resection of the stomach. Biopsy report: large saddle ulcerating tumor on the lesser curvature and convolutional type of gastric mucosa. Lymphoblastoma. Autopsy two days later showed no involvement of any other organ.

Case xix (287364). P. C. Male, aged thirty-four. First admitted in 1927 with roentgen diagnosis of benign gastric ulcer of the fundus and marked distortion of the gastric rugae. For six months this patient had had chills, sweats and epigastric pains. The ulcer was resected and the biopsy reported as a benign chronic ulcer. Patient was readmitted January, 1933, for question of gastrojejunal ulcer. He again complained of epigastric pain associated with night sweats and hematemesis. Skin, glands, spleen, liver and temperature not remarkable. Operation showed lymphoblastoma involving the whole stomach which was resected. Resection of the stomach showed convolutional rugae studded with polypoid sessile tumors measuring from 0.5 to 1.5 cm. Postoperative death.

SUMMARY OF THE CASES REPORTED FROM THIS HOSPITAL

Age and Sex. The series of cases from this hospital contains 6 females and 13 males. Only 1 case was under thirty years of age and only 1 case past seventy years. Five were in the age group thirty to forty-nine, and 12 were in the group of fifty to seventy years.

Signs and Symptoms. Seven cases gave a history of colic and diarrhea, and 3 of colic and constipation. There were 3 cases with typical histories of peptic ulcer. It is interesting to note that over half of the patients gave one or more of the characteristic symptoms of lymphoblastoma, such as sweats, pyrexia, superficial glandular enlargement, palpable spleen, skin changes, etc., which rarely occur with ordinary gastrointestinal lesions. Only 7 of the patients showed a positive guaiac test or tarry stools, and of the 19 patients studied, 15 had a red blood count of over four million.

Roentgen Diagnosis. One-half of our cases showed involvement of both the stomach and intestine, and in one-half of these, the lymphoblastoma had involved both the gastric and duodenal side of the pyloric valve. We were unable to find cancer of the lower end of the stomach which had infiltrated across the pylorus to involve the duodenum. In our series, the gastric rugae were not remarkable in those cases which involved the lower half of the intestinal tract, but in those cases involving the stomach, the gastric mucosa was altered in 75 per cent. In 25 per cent of this latter group, the mucosal folds were convolutional in type. So far we have been unable to differentiate the appearance of the mucosa from that of gastritis. At operation, the cases of gastritis showed reddened inflamed mucosa while those of lymphoblastoma were dirty gray in color.

Any improvement in the roentgenological diagnosis of gastrointestinal lymphoblastoma must come through familiarity of the roentgenologist with the findings of the pathologist, and with this thought in mind, both the clinical and pathological reports have been studied. The important roentgen finding in the diagnosis of gastrointestinal lymphoblastoma becomes appar-

Fig. 1. Lymphoblastoma involving both the pylorus and duodenum. Convolutional hypertrophy. Patient received recurrent radiation therapy over abdomen for two years with relief of abdominal symptoms. Case proved by autopsy.

ent from a careful review of the gross pathological findings in the 88 cases found in the literature and the 19 cases from this hospital.

DISTRIBUTION OF LESIONS IN THE GASTRO-INTESTINAL TRACT

Cases	Stomach Alone	Stomach and Intestine	Intestine Alone
88 (in literature)	24 (27%)	21 (24%)	43 (49%)
19 (from Massachusetts General Hospital)	4 (21%)	9 (47.6%)	6 (31.5%)

The stomach was involved in one-half of the cases. In 12 reported cases, the disease was primarily in the stomach and entirely localized in this organ, an important finding, as surgical removal offers a definite possibility of cure. Vasiliu reported 1 case with a five year follow up and no recurrence. The case of Singer did not survive operation but the histological examination showed the lesion to be entirely limited to the stomach.

Most of the gastric lesions were described as resembling ulcers, polyps, or cancers. Three cases were described as resembling 'linitis plastica." In one-third of the cases in which the stomach was involved, the pathologist described marked thickening and distortion of the gastric rugae, its folds becoming so distorted that they resemble the cerebral convolutions, and were called "convolutional" or "gyroscopic." We have found this marked distortion of the rugae of great value in the roentgen diagnosis. The convolutional type of rugae occurs in 17 per cent of all the cases of gastrointestinal lymphoblastoma.

In 21 cases, both the stomach and intestines were involved. Of these, 16, or 18 per cent, of all the reported cases showed a lesion in the stomach associated with duodenal ulceration. The frequency with which this disease extends beyond the pylorus to involve the duodenum is in marked contrast to cancer of the stomach which rarely involves the duodenum. According to the best pathologic data, in only 5 per cent of the cases does cancer spread beyond the pylorus to involve the duodenum, whereas in 75 per cent of the cases of lymphoblastoma involving the lower end of the stomach we find involvement of the duodenum reported. As a consequence of this finding, we mention the possibility of lymphoblas-

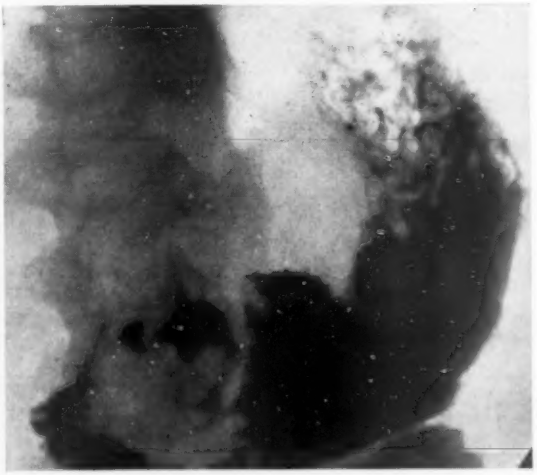

Fig. 2. Lymphoblastoma of stomach spreading from pylorus into duodenum.

toma whenever the roentgen examination shows a double lesion around the pyloric valve involving both the stomach and duodenum, and make a definite diagnosis of lymphoblastoma if this finding is associated with marked thickening and distortion of the gastric rugae.

When the lesion is located in the ileocecal region, it is not uncommon for it to produce mandarin-sized tumors which may cause invagination of the ileum into the cecum. The mucous membrane of the cecum usually shows thickening and distortion like that of the stomach. With the exception of this distortion and thickening of the mucous membrane of the cecum, a review of the pathological findings reveals no facts of diagnostic importance. It is stated that tuberculosis attacks the lower small bowel more frequently than the upper and that lymphoblastoma attacks the upper small bowel rather than the lower. A review of the cases with this in mind gave no conclusive facts. On the contrary, it was not rare to find both tuberculous and lymphomatous ulcers side by side in the same part of the intestine. The small and large bowel were both involved in about the same percentage of cases as were those of the stomach and small bowel. A not uncommon combination and found in lymphoblastoma of the gastrointestinal tract

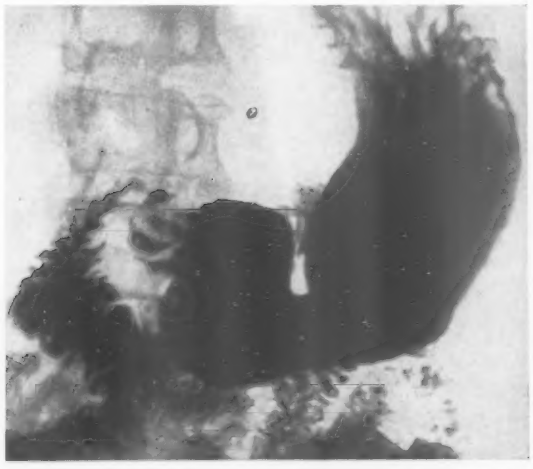

Fig. 3. Same case as Figure 2 after completion of radiation therapy.

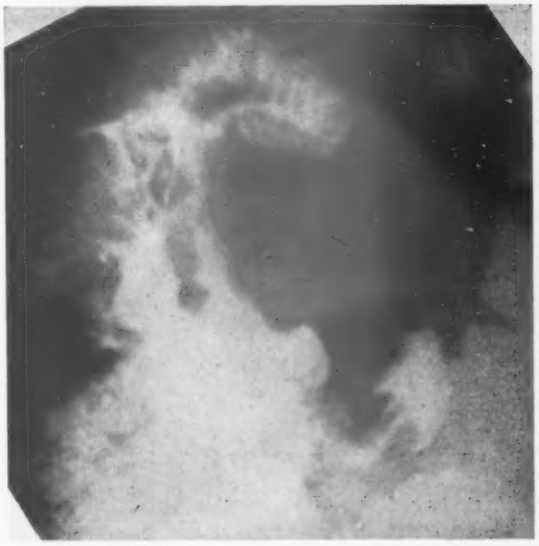

Fig. 4. Gastric lymphoblastoma with ulceration of lesser curvature and convolutional type of rugae.

was a duodenal ulceration and a rectal stricture. Thus the roentgenologist should find a multiplicity of lesion in about 50 per cent of his cases of lymphoblastoma.

Lymphoblastoma has been found as a primary lesion in all parts of the gastrointestinal tract except the esophagus. In this organ, it may appear as a direct extension from a lesion in the stomach or from the epiglottic folds. The majority of the lesions are found around the pylorus and ileocecal region. When found around the pylorus, there is a marked tendency for the disease to spread beyond the pyloric valve and involve the duodenum. The great majority of the lesions start in the submucosa. Of great diagnostic importance to the roentgenologist is the pathologist's description of the mucous membrane of the involved stomach. In 70 per cent of the cases, the rugae of the stomach were described as thickened and distorted, and in 35 per cent the rugae were so greatly distorted that the pathologist described them as resembling the cerebral convolutions.

It has been a rare experience at this clinic to find a gastric cancer which infiltrated beyond the pylorus and produced a deformity of the duodenal cap. On the other hand, we have frequently found

Fig. 5. Gastric lymphoblastoma with large shallow ulceration on lesser curvature and gross thickening and distortion of rugae.

lymphoblastoma of the lower end of the stomach infiltrating beyond the pyloric valve to involve the duodenum. The malignant posterior wall ulcers that perforate into the pancreas may produce a deformity of the duodenal loop giving the appearance of multiple lesions of lymphoblastoma. However, the lymphoblastomas that we have reviewed that had progressed this far have all shown some of the other diagnostic signs of the disease, such as the distortion of the rugae, pressure defects by an enlarged spleen, displacement of the stomach gas bubble away from the left diaphragm, or changes in the chest consistent with lymphoblastoma. Autopsies have shown that the displacement of the fundus of the stomach was due to one of several causes such an enlargement of the liver, spleen, or retroperitoneal glands, and in 2 cases the left diaphragm was found to be over an inch in thickness as a result of infiltration with lymphoblastoma. The displacement of the fundus and gas bubble have been found in other diseases that involve the liver and spleen, but these are not associated with convolutional gastric rugae. In 1,000 routine autopsies at this hospital, in all cases that showed enlargement of the liver and spleen associated with gastric convolutional rugae, histological examination has shown the presence of lymphoblastoma with the following exception. This was a case with a vascular engorgement of the gastric mucosa from thrombosis of gastric vessels. The involved cecum shows the same type of thickening and distortion as the gastric mucosa. With the newer compression technique, we hope to demonstrate this change roentgenologically in cases of lymphoblastoma involving the ileocecal region as consistently as we now do changes in the gastric mucosa.

The anatomical changes that are of value to the roentgenologist in gastrointestinal lymphoblastoma are thickening and dis-

Fig. 6. Rectosigmoid stricture with obstruction. Proctoscopic biopsy showed lymphoblastoma. Patient entirely relieved for three years by recurrent radiation therapy.

tortion of rugae; displacement and pressure defects of the fundus; a double lesion of the gastrointestinal tract; a lesion of the pylorus that extends over the valve and involves the duodenum; and changes in the duodenal loop associated with pressure defects on the fundus of the stomach and splenic flexure (enlargement of the head of the pancreas associated with an enlarged spleen).

This summary of the above anatomical findings has now been used by the six roentgenologists of this hospital for two years. We have been able to make a definite diagnosis of gastrointestinal lymphoblastoma in 5 cases which were subsequently confirmed. In 4 other proved cases, we mentioned lymphoblastoma as a possibility. Reviewing these cases, it has been found that in all the proved cases of gastric lymphoblastoma, the gastric rugae were thickened and distorted; on the other hand, those cases in which a roentgenological diagnosis of gastric lymphoblastoma was suggested as a possibility by the presence of a double lesion and the subsequent biopsy disproved the diagnosis, the gastric rugae were not grossly distorted.

THERAPY

The treatment of gastrointestinal lymphoblastoma usually requires both surgery and deep roentgen therapy. Surgery offers a definite possibility of cure. The literature contains at least one surgical cure for gastrointestinal lymphoblastoma of the Hodgkin's type. This was a medical student operated upon by Vasiliu and followed for five years without any evidence of recurrence. The case reported by Singer would have been another had he survived the operation as autopsy with microscopic examination of all tissues showed the lesion completely localized to the stomach. The records of this hospital also show 1 case of lymphoblastoma of the intestine surgically removed and a five year follow up shows no evidence of recurrence. These 3 cases offer excellent proof that surgical cure is possible when the disease is entirely localized to one organ. However, the literature reveals the fact that many cases thought to have been entirely localized to the gastrointestinal tract at operation later showed metastases in other organs. Thus the case of Steindl recovered from the surgical removal and subsequently showed involvement of the hilus glands. Warfield and Kristjanson found microscopic involvement of the spleen at autopsy following the surgical excision of gastric lymphoblastoma of the Hodgkin's type. The autopsy findings on the case of Pokitilo and Busni after surgical removal of an ileocecal tumor showed a metastatic nodule in the spleen not noted at operation. Biebl's case remained alive for four years but required a second operation for excision of a recurrence. Another case reported by Ogloblina was successfully operated upon and remained well for eight months at which time death occurred from a perforating lymphoblastomatous duodenal ulcer. The reported cases of Neuber, Froboese, de Groot, Redwitz and others, are not accepted as cures since the cases were not followed for five years. On the other hand, the cases that survived operation were greatly benefited. Most of the cases were poor surgical risks and death from perforating ulcers would probably have followed had no surgical treatment been attempted. Whenever lymphoblastoma is limited to the gastrointestinal tract, we feel that surgical excision should be attempted, but when the lesions are multiple showing that the disease is generalized, deep roentgen therapy is superior to surgical interference. If the patient is explored and the lesion removed, he should have roentgen treatment before he is discharged and should be seen by the roentgenologist about every two months for further treatment and examination for recurrence or metastases.

The work of Chaoul and Lange would seem to indicate that the best method of high voltage therapy for gastrointestinal lesions consists of large fields and small dosages over a long period of time. In their reported series of cases, they obtained

cures that up to the time of publication lasted about three years. Sternberg reported a case in which high voltage therapy caused a complete disappearance of the enlarged hilus glands but after a six year follow up without any evidence of recurrence in the chest, the patient suddenly developed gastric symptoms and microscopic sections showed lymphoblastoma of the Hodgkin's type involving the stomach. In the cases treated at this hospital under the direction of Dr. Holmes, large fields and suberythema dosages of approximately 600 r each, to the front and back of the abdomen, in daily doses of 200 r have been the rule. This general plan of treatment usually causes the disappearance of the tumor and great relief to the patient. One of our cases has been on this general plan for five years; another case with lymphoblastic strictures of the rectum and duodenal ulceration has received this treatment for two years with complete relief of obstruction and bleeding.

REPORTED CASES OF GASTROINTESTINAL LYMPHOBLASTOMA (HODGKIN'S TYPE)

Gastric Cases with the Disease Completely Localized to the Stomach. One case each reported by Steindl, Neuber, Kan, Redwitz, Froboese, Thiemer and Singer. Two cases by Behring. Three cases by Junghagen.

Cases in Which the Disease Was Entirely Localized to the Stomach and Intestine. One case each by Schlagenhaufer, de Groot, Terplan and Wallesch, Drope, Busni, Behring and Vasiliu.

Gastric Cases with Minor Lesions Outside the Gastrointestinal Tract. One case each by Scott and Forman, Sternberg, Vasiliu and Sussig. Cases I and II of Coronini's series belong to this group.

Gastric Cases with Major Lesions Outside the Gastrointestinal Tract. One case each by Reimann and Lichtenstein. Two cases by McAlpin and von Glahn. Two cases by Terplan and Mittelbach.

Cases with Gross Lesions of Both the Stomach and Intestine and Minor Involvement of Other Organs. One case each by Schlagenhaufer, Terplan, Sussig, Novotny, Kaznelson, McAlpin and von Glahn and Junghagen.

Cases with Generalized Involvement and Lesions Present in Both the Stomach and Intestine. One case each by Weinberg, Russell, Hauck, Coronini, Tschilow. Two cases in the series of Terplan and Mittelbach.

Intestinal Cases with no Involvement of the Stomach or Other Organs. Eberstadt, Catsaras and Georgantas, Partsch, de Groot, Pamperl and Terplan, Heinmann-Hatry, Biebl, de Jong, Lange, Pissarewa, Kan, Pokotillo, Schegelew, Ogloblina, Stoerch, Sussig, Hellmann, Wald, Nowicki, Venables, Vasiliu, Hanneborg and Wahlgren.

Intestinal Cases with no Involvement of Stomach and Generalized Involvement. Ziegler, Schlagenhaufer, Urchs, Terplan and Mittelbach, Stahr and Synwoldt, Warfield and Kristjanson, McAlpin and von Glahn, Cracium, and Ceelen and Rabinowitsch.

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THE SMALL INTESTINE AND DIARRHEA*

By ROSS GOLDEN, M.D.
NEW YORK CITY

INTRODUCTION

DIARRHEA, with or without abdominal pain, is an important symptom which usually brings to mind the possibility of disease of the large intestine, and the patient is correctly referred for a barium enema. The failure to demonstrate disease of the colon does not necessarily mean that no organic basis exists for the symptoms. It is frequently forgotten that disturbances of the small intestine also may cause diarrhea.

The terms used in textbooks of medicine (e.g., Cabot, Osler, French) indicate that certain concepts of the causes of diarrhea are quite clear-cut but that many are quite hazy and indefinite. Apparently "enteritis" is likely to be used when an etiological diagnosis cannot be made. It may therefore be useful to classify the causes of diarrhea from the anatomical standpoint; that is, as to whether the origin of the disturbance is in the large or the small intestine. This may aid in considering the etiological possibilities and in selecting the roentgen and laboratory procedures suitable to the case.

The purpose of this paper is to emphasize the fact that the small intestine may be the source of the trouble and deserves study by roentgen methods when the large intestine is found to be normal, and to discuss briefly the diseases demonstrable by this means. The acute diarrheas lasting only a day or two, apparently due to so-called food poisoning, are not included; an opportunity to examine such a case by roentgen methods has never presented itself.

TECHNIQUE

Disease of the ileum is occasionally disclosed when the opaque material used for the barium enema flows back through the ileocecal valve. Whenever the possibility of disease of the small intestine presents itself, however, it is important to make a special examination of the jejunum and ileum with a barium suspension given by mouth.

Two ounces of barium sulphate mixed with water is given on an empty stomach the first thing in the morning. With the patient in the prone position, films of the abdomen are taken at intervals of half an hour, in some cases fifteen minutes, until the barium reaches the ascending colon or until adequate information concerning the small intestine is obtained. It is sometimes helpful to have exposures of certain loops on small films at intervals of five or ten minutes. Films at five, six, nine and twenty-four hours are taken routinely. Plain screens permit exposures of 1/10 sec. with 100 ma. and the voltage according to the thickness of the patient. Ravdin, Pendergrass, Johnston and Hodes prefer to use the Potter-Bucky diaphragm which requires a longer exposure. Roentgenoscopic observations of intestinal movements and mobility, tenderness, etc., are made two or three times during the examination. The details of the procedure must necessarily be varied from case to case.

Ravdin, Pendergrass, Johnston and Hodes believe that a plain barium-water mixture should be used, rather than a more complicated suspension, to avoid any possible effect on the emptying of the stomach or allergic reaction on the intestine.

THE NORMAL SMALL INTESTINE

A satisfactory review of the normal small intestine cannot be made here (see Ravdin et al., Cole, and Menville and Ané). Important points may be mentioned briefly. The barium shadow is usually continuous and not scattered and divided. The lumen

* From the Departments of Radiology of the Presbyterian Hospital and of the College of Physicians and Surgeons, Columbia University, New York.

may vary from 1.5 to 3 cm. in width. The mucosal elevations of the jejunum are very high, giving its shadow a fine feathery appearance; they become less and less marked in the lower segments. In the ileum their indentations are more widely separated and are hardly more than 1 mm. high; they usually run at right angles to the long axis of the intestine but occasionally lie parallel with it. The wall of the normal small intestine is so soft and flexible that it cannot be palpated; it is freely movable and not tender. The peristaltic contractions seldom exceed 1 cm. in width, are sharply demarcated, and are promptly followed by relaxation to the normal width of the lumen.

In our experience the opaque material begins to pass through the ileocecal valve in from one and a half to four hours after ingestion if the stomach begins to empty promptly in apparently normal individuals. The lower ileum still contains barium at six hours but should be empty at nine hours.

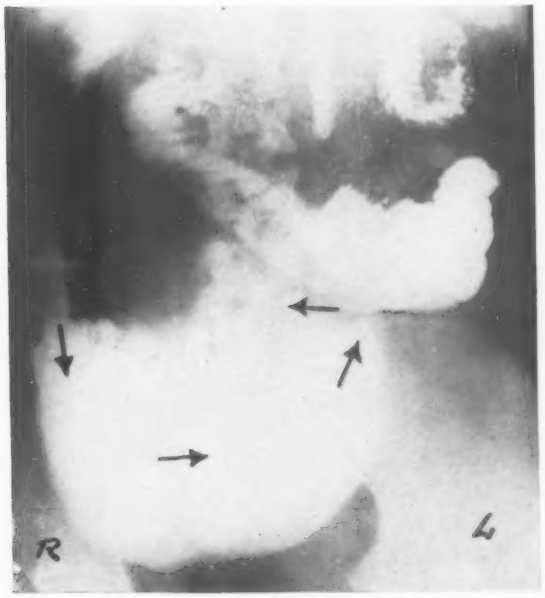

Fig. 1. *Nonspecific Granuloma of the Ileum.* A woman, aged twenty-four, had diarrhea and abdominal pain for ten years. The barium enema fluid flowed into the terminal ileum, outlining the dilated portion shown above. The loops leading into and out of this had abnormal wall contours. The arrows point caudad. The film reproduced above was taken two and a half hours after the ingestion of barium. The dilated loop was resected (see Figs. 2 and 3). Following operation the patient improved rapidly but temporarily developed signs of pellagra (see Eusterman and O'Leary).

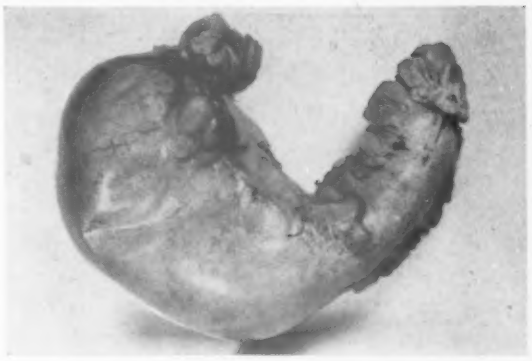

Fig. 2. *Nonspecific Granuloma of the Ileum.* (The same case as in Fig. 1.) The resected specimen measured 40 cm. along its antimesenteric border and 15 cm. along its mesenteric border. It held 700 c.c. The wall of the dilated portion was very thin, while that of the proximal loop was thickened. Scarred areas were present on the surface. There was no constriction of the lumen amounting to obstruction (see Fig. 3).

NONSPECIFIC GRANULOMA OF THE SMALL INTESTINE

This term is meant to include "regional ileitis" (Crohn, Ginzburg and Oppenheimer), "cicatrizing enteritis," etc. The disease is apparently due to an unknown infection of the wall of any portion of either small or large intestine which produces thickening and ulceration of the mucous membrane, hypertrophy of the muscularis, infiltration with round cells, fibrosis, later fistula formation between loops of small intestine, between small and large intestine or between intestine and skin; it may cause intestinal obstruction. It is frequently associated with marked mesenteric lymphadenitis. The lower part of the ileum is more frequently involved than any other portion of the intestinal tract and the disease does not often attack the cecum.

Diarrhea was either the presenting or an important symptom in 9 of 11 cases observed at the Presbyterian Hospital. Most of these patients were referred to the De-

FIG. 3. *Nonspecific Granuloma of the Ileum.* (The same case as in Figs. 1 and 2.) Serpiginous branching ulcerations were present on the mucous membrane and small polypoid masses of granulation tissue were present in the proximal end of the dilated portion of the ileum.

partment of Radiology first for examination of the large intestine.

The roentgen evidence of the disease in the well-advanced cases was usually narrowing and irregularity of the lumen of several centimeters of lower ileum, with a nine hour ileal residue. In a child, aged six, who had diarrhea with blood and mucus with a negative tuberculin test, the shadow of the terminal 6 to 8 cm. of ileum, although normal in width, contained small rounded areas of diminished density suggesting polypoid elevations on the mucosa and fine irregularities of the margin suggesting small ulcerations. In the earliest case, several roentgen examinations disclosed only spasm, abnormal peristalsis and tenderness of the terminal ileum; the diagnosis was made on the basis of histologic changes in the resected specimen.

Three cases were of unusual interest. The patients were young women who had diarrhea and abdominal pain for ten years (Figs. 1, 2 and 3), three years (Fig. 4), and eight months (Fig. 5), respectively. All were puzzling clinical problems, and psychic disturbances were thought probably to be responsible until roentgen studies disclosed evidence of disease of the small intestine. Two were referred for examination of the colon, but in the third and most recent case, a study was immediately made of the small intestine. In one instance the barium enema material flowed through the ileocecal valve and outlined the tremendously dilated loop of ileum shown in Figures 1, 2 and 3. In the other case, the negative colon examination was followed by months of futile psychotherapy before the patient was referred for study with a barium meal. It is of particular in-

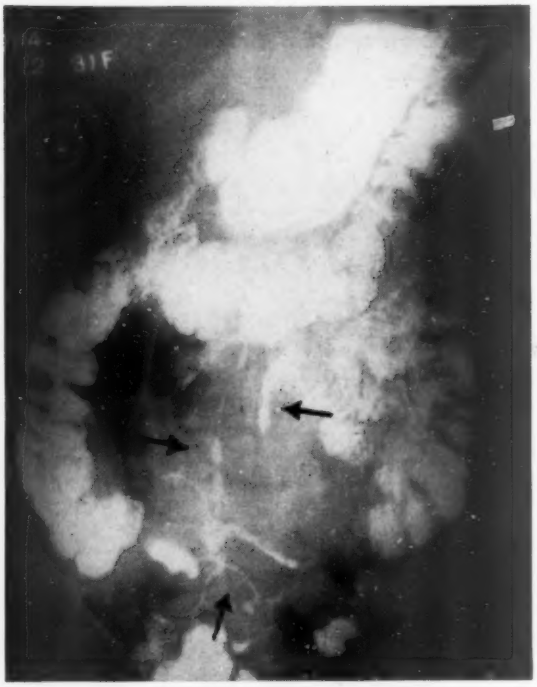

FIG. 4. *Nonspecific Granuloma of the Jejunum.* A girl, aged nineteen, had diarrhea and abdominal pain for three years. A barium enema disclosed nothing abnormal. She was given psychotherapy for several months before the narrowed loops of lower jejunum (arrows) were demonstrated following a barium meal. At operation several thickened loops of lower jejunum were covered with small tubercle-like elevations. Both surgeon and roentgenologist thought this was tuberculosis. One of the small tubercle-like elevations was examined microscopically and interpreted by the pathologist as nonspecific granuloma of the intestine.

terest that diarrhea was an important symptom in the presence of sufficiently delayed motility, if not obstruction, to produce the dilated loops shown in Figures 2 and 5.

TUBERCULOSIS OF THE INTESTINE

Tuberculosis of the intestine is usually associated with phthisis but may occur in the absence of pulmonary disease. Both ileum and cecum are usually involved. In rare cases a large localized tuberculous ulcer may be found in the large intestine. Of 184 cases of pulmonary tuberculosis with intestinal lesions observed at necropsy by Brown and Sampson, 11 (6 per cent) had them only in the small intestine, and 35 (19 per cent) only in the large intestine. Ulceration of the mucous membrane, and infiltration and fibrosis of the wall are the important pathologic manifestations of the disease.

The roentgen-ray evidence of ileocecal tuberculosis has been described in detail by Brown and Sampson and numerous other writers. In brief, it consists primarily of irritability and hypermotility of the ileum and cecum, and deformity of the wall of the involved region which are better demonstrated by ingested barium than by the enema. Nonspecific granuloma of the ileum, which is to be differentiated, involves the cecum infrequently; the diseased portion seems less irritable and more likely to retain the barium. However, in occasional cases the differential diagnosis may be difficult from the barium examination alone. The presence of phthisis and, in children, a positive tuberculin test suggest tuberculosis.

Diarrhea is not as frequent in ileocecal tuberculosis as in nonspecific granuloma of the intestine. The incidence of this symptom as reported by different writers varies. Either continuous diarrhea or alternating diarrhea and constipation was present in 54 per cent of the 233 cases reported by Kline and in 27 per cent of 36 cases described by Logan. Of 100 cases with positive roentgen evidence of this disease

FIG. 5. *Nonspecific Granuloma of the Ileum with Obstruction.* A woman, aged twenty-six, had severe diarrhea and abdominal pain for eight months. The small intestine study disclosed evidence of obstruction in the ileum. The narrowest diameter in the constricted area of the resected specimen, shown above, measured 0.5 cm. The wall of the dilated portion was hypertrophied. Several ulcerations of the mucous membrane were present.

studied by Erickson at the Trudeau Sanatorium, 66 had diarrhea, while Blakie and Laird found it in only 27 per cent of 44 similarly diagnosed cases. It was present in 8 of 14 cases at the Presbyterian Hospital. In one case this disease was associated with carcinoma of the ileum with metastases, proved by histologic study of the resected specimen; it is of interest that this patient showed no clinical or roentgenological evidence of pulmonary tuberculosis.

DEFICIENCY DISEASES

Chronic steatorrhea, non-tropical sprue, celiac disease in infants, adult celiac disease, tropical sprue are all apparently based upon the same physiological disturbance—a lack of an essential substance or substances—and may be considered as essentially the same disease (Thaysen); all have diarrhea as the presenting symptom. It is of interest that not all patients respond to the same treatment. It is not necessary here to discuss the details of the pathogenesis and clinical course of these diseases or the various opinions concerning them.

Snell and Camp (1934) pointed out some

FIG. 6. *Deficiency State (non-tropical sprue).* A man, aged thirty-four, complained of diarrhea and loss of weight of two months' duration. The barium meal shows marked smoothing of the walls of the jejunum with slight dilatation and hypomotility. The symptoms were promptly relieved by the injection of liver extract (see Fig. 7).

significant changes in the wall of the upper part of the small intestine on roentgen examination in cases of chronic steatorrhea, namely (1) coarsening of the mucosal markings of the duodenum and jejunum, (2) obliteration of the mucosal markings and smoothing of the walls especially in the jejunum with the formation of smooth sausage-like masses of barium, (3) dilatation of the jejunum, and (4) hypomotility of the small intestine (Fig. 6). As an explanation for these findings, Snell, Camp, and Watkins (1935) suggest edema of the mucous membrane and in more severe cases atrophy or destruction of the mucosa; they describe a change toward the normal coincidentally with clinical improvement. They note that the stomach, ileum and colon may infrequently be involved. They believe that these changes may be present in other conditions.

Mackie and Pound (1935), and Mackie, Miller and Rhoads (1935) describe very similar, if not identical, changes in the small intestine demonstrable by roentgen methods in typical cases of tropical sprue and in the deficiency states associated with severe chronic colitis. They emphasize the tendency to form segmental pockets of barium as a manifestation of disturbed intestinal motility.

Another sign observed in 3 adults with chronic steatorrhea at the Presbyterian Hospital and in several infants with a diagnosis of celiac disease at the Babies Hospital was the flocculation of the barium in the ileum, the tendency to form small rounded or oval flecks of barium instead of the smoothly homogeneous continuity of the barium shadow as seen under normal conditions (Fig. 7). The possibility that

FIG. 7. *Flocculation of the Barium in Deficiency States.* A film six hours after a barium meal (same patient as in Fig. 6) shows the granular, flocculent appearance of the barium shadows noted in a number of adults and children with deficiency states, which is in marked contrast to the usual homogeneous appearance of the shadow of the barium-filled intestine under normal conditions. The hypomotility is shown by the fact that little if any barium has entered the cecum in six hours.

abnormal fat digestion with abnormal quantities of fat, fatty acids or soaps, or some other abnormal non-opaque material in the intestine might be responsible for this is suggested.

Films were available showing barium in the small intestine in 11 cases of celiac disease in infants at the Babies Hospital. In 7 of the 11, definite changes of the nature of those mentioned above were apparent in the jejunum. In 4 cases the coarsening of the mucosal folds in the jejunum was so slight as to be doubtful but in 2 of the 4 the duodenum appeared abnormally smooth.

Changes identical with those described by the above-mentioned writers were noted in 3 adults with chronic steatorrhea at the Presbyterian Hospital; the injection of liver extract was followed by prompt improvement in 2 of them, but not in the third who grew better slowly on a banana diet. Identical changes were also demonstrated in the small intestine of 2 other adult cases of chronic or recurrent diarrhea, in which the clinical classification was not as definite as in the 3 cases just mentioned; they are still under observation.

The diagnosis of this condition is usually made by clinical methods. However, in the presence of an incomplete clinical work-up or an atypical clinical picture, the first suggestion of the possibility of a deficiency state may come from a study of the small intestine; an example was 1 of the 2 above mentioned patients who responded to liver extract and who was admitted to the hospital with a diagnosis of pancreatic insufficiency made at another institution (Fig. 8).

FIG. 8. *Deficiency State.* A woman, aged fifty-five, had intractable diarrhea and loss of weight for two months. A diagnosis of pancreatic insufficiency was made in another institution. The small intestine study disclosed marked smoothing of the jejunum with hypomotility, leading to the diagnosis of a deficiency state. The symptoms were promptly relieved following the injection of liver extract.

UNCLASSIFIED "NERVOUS" DIARRHEA

Diarrhea sometimes occurs without either clinical or roentgen evidence of organic disease. The symptom is usually attributed to psychic or nervous influences. The following case appears to be an example of this condition; the roentgen studies disclosed marked deviation from the normal in physiology but no evidence of actual disease of the intestinal wall was forthcoming:

(Unit No. 491635). A highly intelligent business man, aged forty-three, was admitted in June, 1936, for study because of a painless diarrhea of six years' duration. The symptom began shortly after the stock market crash in 1929, although the patient maintained his business and improved his situation during the depression. He averaged four to six loose bowel movements a day with no pain or other symptoms. He was well developed, slender and had lost 10 pounds during the six months previous to admission. The physical and laboratory examinations disclosed nothing remarkable except a persistent bradycardia, the pulse rate averaging around 60. The barium enema disclosed nothing abnormal. The small intestine study disclosed unusual hypermotility of the jejunum and ileum. The barium reached the cecum in forty-five minutes and the ileum was empty in three and a half hours. The jejunum showed nothing remarkable. The lumen of the ileum was rather narrow; hyperactive peristalsis and numerous spastic contractions

FIG. 9. *"Nervous" Diarrhea with Hypermotility of the Small Intestine.* A man, aged forty-three, had painless diarrhea for six years and bradycardia. Ingested barium began to enter the cecum in forty-five minutes and the ileum was empty in three and a half hours. No evidence of organic disease was demonstrated. The film reproduced above was taken at one hour and shows the numerous irregular contractions in the ileum noted at several roentgenoscopic observations.

were present (Fig. 9). There was no tenderness anywhere in the abdomen. A repetition of the examination three days later produced almost identical findings. There was nothing which could be interpreted as evidence of organic disease of the intestinal wall. The large intestine showed no evidence of irritability. The patient was put on a bland diet, was given atropine, tobacco was eliminated and the possible psychic origin of the disturbance was discussed with him frankly. During 2 weeks' rest in bed in the hospital, the diarrhea ceased and the patient began to regain his lost weight rapidly.

Comment. If the diarrhea in this case were due to organic disease of the intestine, it would seem that evidence of it should be demonstrable after six years. The patient apparently was suffering from vagotonia. The trouble seemed to originate in the psyche or the nervous system; the mechanism appeared to be a disturbance in the physiology, a definite hypermotility of the small intestine, particularly the ileum.

LYMPHOSARCOMA OF THE SMALL INTESTINE

Diarrhea seems to be infrequently associated with lymphosarcoma of the small intestine. Of the 11 cases described by Oberndorfer in which a clinical history was mentioned, diarrhea was present in only 1 instance in which the growth had involved the pancreas. Zimmer mentions 2 cases without this symptom. However, it was present in 3 of 5 cases in the records of the Presbyterian Hospital. In these 3 cases the disease was extensive and advanced instead of localized, as it apparently was in Oberndorfer's reports.

Lehmkuhl (1927) described a case in which lymphosarcomatous infiltration was present throughout the entire small intestine with many undermined ulcers up to 3.5 by 4 cm. in size. The mucosa was level and thickened; no normal folds were present. The mesenteric lymph nodes were enlarged. The patient was a woman, aged thirty, with a two year history of cramping left upper quadrant pain and diarrhea, at first coming on just before the menses but becoming continuous later. The stools were foul, foamy and contained an excess of fat, fatty acids and undigested muscle fibers, but without mucus or blood. The clinical diagnosis was pancreatic insufficiency. No mention is made of a roentgen examination. This writer states that he was unable to find a similar case in the literature.

The following case is almost the duplicate of that reported by Lehmkuhl and again illustrates the importance of investigation of the small intestine of patients with diarrhea when the large intestine is normal.

(Unit No. 387109). A woman, aged thirty-four, was admitted to the Presbyterian Hospital August 8, 1933, because of intractable diarrhea of four years' duration. Five years previously splenectomy was performed for purpura

hemorrhagica with relief of all symptoms. On admission she weighed only 80 pounds. Her stools were described as "sprue-like," foul, soapy, at times containing fat globules. The blood examination disclosed nothing abnormal except 20,000 white cells with 80 per cent polymorphonuclear leukocytes. A barium enema disclosed nothing abnormal except hypotonicity of the large intestine. A study of the small intestine (Fig. 10) disclosed a very patchy irregular distribution of the barium throughout the jejunum and upper ileum. The wall markings of the jejunum were low, coarse, irregular and widely separated. Almost the entire small intestine remained filled at eight hours. The significance of these changes was not understood at that time. The patient died August 23, 1933.

At necropsy (No. 11311) the duodenal folds beginning about 4 cm. below the stomach were very prominent, thick, almost polypoid. The mucosal folds of the proximal 10 cm. of the jejunum were similar (Fig. 11). This thickening was confined to the mucosa. The mesenteric lymph nodes were enlarged throughout. The lower jejunum, ileum and large intestine appeared grossly normal. Histologic examination disclosed abnormally dense infiltration of the duodenal mucous membrane with large and small round cells. The latter had deeply basophilic nuclei and the former large, pale, irregular vesicular nuclei. Very few mitotic figures were seen. In the jejunum and ileum the same cellular infiltration of the mucosa was present, decreasing in the more caudad portions. Similar cells were found in the mesenteric lymph nodes but were not present in the one inguinal node examined. Many of the cells contained intranuclear inclusions of eosin-staining material, distending the nucleus and crowding the chromatin against the wall. In some cells this material was fragmented and in others it had ruptured the nuclear membrane with dissolution of the cell. The pathologist classified this case as lymphosarcoma of the intestine.

Fig. 10. *Infiltrating Lymphosarcoma of the Small Intestine.* A woman, aged thirty-four, had intractable diarrhea for four years with great loss of weight. The film taken five hours after a barium meal shows a very patchy irregular distribution of barium throughout the small intestine with abnormal wall patterns and with marked hypomotility (see Fig. 11).

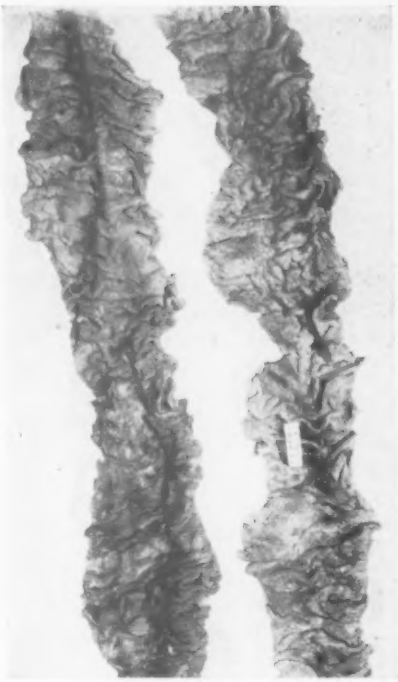

Fig. 11. *Lymphosarcomatous Infiltration of the Small Intestine.* The marked thickening and widening of the mucosal folds of the jejunum were due to lymphosarcomatous infiltration. The muscularis was intact. The mesenteric lymph nodes were greatly enlarged.

Comment. The stools in this as well as in Lehmkuhl's case had many of the charac-

teristics of those of the deficiency states discussed above. It seems quite possible that the diarrhea was due to a disturbance in the digestion and absorption of fat and of essential substances caused by the infiltration of the wall of the small intestine, and giving the stools their sprue-like character. The infiltration was probably responsible for the abnormal wall pattern of the jejunum and, together with the mesenteric lymphadenitis (Golden), for the hypomotility. It should be noted that the muscularis was intact.

A number of writers comment on the fact that the portions of the intestine involved by lymphosarcoma are dilated rather than constricted.

NEOPLASMS OF THE SMALL INTESTINE

Diarrhea did not occur in any of the 11 cases of assorted benign neoplasms of the small intestine found at necropsy in the Department of Pathology of the Presbyterian Hospital.

In 20 cases with proved malignant disease of the small intestine, other than lymphosarcoma (carcinoid 8, carcinoma 9, sarcoma 2, perithelioma 1), diarrhea occurred in only 4. Three of these patients had carcinoid of the ileum with extensive metastases at autopsy; diarrhea had been present three years, nine months, and ten weeks, respectively, before admission. The last mentioned patient had intestinal obstruction with marked dilatation of the jejunum. The reason why these 3 patients had diarrhea and the others did not is not clear. The fourth patient had the combination of ileocecal tuberculosis and carcinoma of the ileum, mentioned above, and it seems more likely that the former was responsible for the symptom under discussion.

In 6 of the 20 cases no barium studies of any sort were done. Eleven of them had an ordinary gastrointestinal series in which no particular attention was paid to the small intestine but abnormalities of the jejunum or ileum were detected or are demonstrable on the films in 9. Two of the 3 carcinoid cases with diarrhea were given only barium enemas and no lesion was demonstrated. Studies of the small intestine in the 2 most recent carcinoid cases disclosed the disease.

Space does not suffice here for a satisfactory discussion of the roentgenology of malignant neoplasms of the small intestine. It is hoped to present a study of these cases from that point of view in a later communication from this department. Suffice it to say that malignant disease of the jejunum or ileum may cause (1) obstruction with dilatation above the growth, (2) localized narrowing of the lumen in which destruction of the mucosal folds may be demonstrated, and (3) intussusception.

No diarrhea was present in a case of nonspecific, unexplained ulcer of the ileum.

It would seem that limited, localized involvement of the small intestine by neoplasms is not likely to be associated with diarrhea.

INTUSSUSCEPTION

Cabot mentions diarrhea as a symptom in 3 of 10 cases of intussusception, the region of the intestine involved not being stated. In 11 cases of intussusception at the Presbyterian Hospital, in which the small intestine was the site of the trouble, diarrhea is not mentioned in the records. Four of the 10 patients complained specifically of constipation. Pain was the outstanding symptom.

DISCUSSION

Cabot remarks that the diarrhea from definite chronic disease may be intermittent and may appear in acute exacerbations.

Probably the most important step in the diagnosis of any disease is to think of it. In routine clinical work pathologic conditions in the small intestine are doubtless missed because the possibility does not come to mind. In going over gastrointestinal films of 6 children under three years of age, which had been made in another institution and called normal, 2 cases were noted with definite changes characteristic of so-called ileitis in middle or lower loops of ileum. Both of these children had been

examined because they had diarrhea.

It seems quite possible that more extensive study of the small intestine when diarrhea is present might throw new light on the physiology and pathology of this symptom.

SUMMARY

1. Diarrhea may be due to disease of the small as well as of the large intestine.

2. Roentgen examination of the small intestine may disclose evidence of:

(a) Nonspecific granuloma of the intestine (ileitis, etc.) in a high percentage of cases of which diarrhea occurs, even in the presence of obstruction.

(b) Tuberculosis of the intestine, in a little more than half the cases of which diarrhea is present.

(c) Changes in the jejunum and ileum in deficiency states, of which diarrhea is the presenting symptom.

(d) Disturbances in physiology of the small intestine with diarrhea of presumed psychic or nervous origin, an instance of which is described.

(e) Changes in the jejunum and ileum in rare cases of infiltrating type of lymphosarcoma of the intestine which causes diarrhea.

3. Diarrhea occurs uncommonly with localized neoplasms of the small intestine, and rarely, if ever, with intussusception in the small intestine.

4. The small intestine deserves investigation by roentgen methods in cases of diarrhea.

My grateful acknowledgments are due to Dr. James W. Jobling, Director of the Department of Pathology, to Dr. A. Purdy Stout, Director of the Department of Surgical Pathology, and to Dr. John Caffey, Roentgenologist of the Babies Hospital, for permission to use the files and material from their respective departments.

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NON-OBSTRUCTING MALIGNANT TUMORS OF THE SMALL BOWEL

A REPORT OF FIVE CASES

By JAMES R. LINGLEY, M.D.
Massachusetts General Hospital
BOSTON, MASSACHUSETTS

MALIGNANT tumors arising in, or involving, the small bowel occur with sufficient frequency to render their roentgen recognition important. The various authors who have reported series of cases of gastrointestinal malignancy have found 2.5 to 6 per cent of these occurring in the small intestine. Judd,[3] in a series of 3,535 cases of gastrointestinal carcinoma, found 1,689 in the stomach, 1,822 in the colon and 24 in the small intestine—a ratio of 1 in the small bowel to 70 in the stomach and 1 in the small bowel to 76 in the colon.

The whole subject of tumors of the small bowel has been amply covered in recent publications by Raiford,[4] Joyce,[2] Judd,[3] Wakeley,[5] Ewing,[1] and others. This report will therefore be confined to a description of the clinical and roentgenological findings in 5 cases which were interesting because they were extraluminal and non-obstructing in type.

The most common roentgenological finding in cases of small bowel tumor, whether they are benign or malignant, is intestinal obstruction. In such cases the roentgen examination is of great value in determining the presence of obstruction and its location, but the actual cause of the obstruction is usually obscure. As pointed out by Raiford and others, however, there is one type of malignant small bowel tumor which is extraluminal and non-obstructive. Arising in the wall of the small bowel, these tumors grow away from the lumen and out into the mesentery, forming large external masses. The lumen of the involved segment, instead of being stenosed and obstructed, is usually irregularly dilated due to necrosis and ulceration within the tumor mass. In such cases the roentgen findings are very characteristic.

In a series of 25 cases of malignant tumor of the small bowel observed at the Massachusetts General Hospital, 18 produced either stenosis or complete obstruction while 7 were non-obstructive in type. Thirteen of these cases on pathological examination were found to be carcinoma and 12 were sarcoma. Of the 7 non-obstructive tumors, 3 were carcinoma and 4 were sarcoma.

The following 5 cases are reported as illustrative of the non-obstructive type:

REPORT OF CASES

CASE 1 (B. M. 14856). A male, white, aged sixty-three, married; entered the hospital July 30, 1934, because of right upper quadrant pain, vomiting, weakness, constipation and tarry stools. On physical examination, he was found to be anemic and to have a mass in the left mid-abdomen.

Laboratory Data. Red blood cells, 2,890,000; white blood cells, 14,000; hb, 50 per cent. Urinalysis negative. Gastric analysis showed no free HCl. Total acidity 8 at the end of one hour. Blood sugar 141 mg. per 100 c.c.

A barium enema passed without obstruction to the cecum and showed that the mass was extrinsic to the colon and lay anterior and medial to its descending portion.

Barium by mouth showed no evidence of disease of the esophagus, stomach or duodenum. Examination after a two hour interval, however, demonstrated a portion of jejunum which was dilated, ragged in contour and which contained a large irregular filling defect. This defect corresponded to the palpable abdominal mass. At the end of six hours, most of the barium had passed the diseased area, indicating only slight delay at this point. At the end of twenty-four hours, there was a trace of barium adherent to the area of ulceration. In view of the above findings, a diagnosis of malignancy of the jejunum was made, possibly lymphoblastoma.

At operation, a tumor the size of a child's head was found in the left upper quadrant. It was freely movable and definitely arose from the jejunum. The tumor, together with a section of jejunum on each side, was successfully removed and an end-to-end anastomosis made.

The patient made an uneventful postoperative recovery and was discharged August 20, 1934.

Pathological report on the section of jejunum was as follows: A section of jejunum 55 cm. in length; 15 cm. from one end there is a large mass measuring 14×8×7 cm. Over this mass the mucosa is widely ulcerated and brown stained. The mass lies almost entirely on the mesenteric side of the bowel. Its outer surface is nodular, the nodules averaging 1 cm. in diameter. The cut surface is boggy and varies in color from white in the deeper portions to greenish brown below the mucosa.

Microscopic: The tumor is composed of somewhat round cells varying in size from that of a lymphocyte to twice that size. The cytoplasm is scant and neutrophilic. The nuclei for the most part are round, occasionally oval, or horse-shoe shaped. Mitotic figures are very numerous. The cells do not look like lymphocytes and a well-marked alveolar arrangement also is against a tumor of the lymphocytic series. A highly undifferentiated carcinoma seems the most probable diagnosis, but exact classification is not possible.

Fig. 1. Case I. Film taken five hours after administration of the motor meal, showing dilated segment of jejunum containing multiple, irregular filling defects. The barium in the colon is a residue from previous examination of the colon.

Fig. 2. Case II. Roentgenogram showing pressure defect on the transverse colon caused by external mass.

This patient re-entered the hospital two months later with neurological symptoms. He failed rapidly and died December 2, 1934. Autopsy demonstrated metastases to peritoneum and brain.

Comment. The roentgen findings in this case were those of an irregularly dilated segment of jejunum containing an irregular filling defect, the whole area corresponding to a large palpable mass. There was no obstruction but barium adhered to the ulcerated surface even at the end of twenty-four hours.

Case II. A white, Italian housewife, aged fifty-two, entered the hospital on April 8, 1935, because of loss of appetite, increasing constipation and loss of 18 pounds in weight. Two months previously she had consulted her local doctor, who found a large abdominal mass

Fig. 3. Case 11. Showing irregular, dilated segment of jejunum, well visualized one-half hour after administration of the barium meal.

and advised operation. Physical examination showed a large mass in the right upper quadrant extending down to the level of the umbilicus. The mass was freely movable, non-tender, with irregular hard surface.

A barium enema examination showed the mass to lie above the proximal half of the transverse colon and to produce a pressure defect on this portion of the bowel (Fig. 2). It was definitely in contact with the colon but did not involve its mucosa.

Barium by mouth showed a normal esophagus, stomach and duodenum. The second and third portions of the duodenum, however, were displaced to the left by the mass. The barium passed readily through the duodenum, entered the jejunum, and passed to a point about 12 inches from the duodenojejunal junction. At this point the jejunum entered the mass and became grossly irregular and dilated (Fig. 3). A large ulcerated area in this region was demonstrated. At the three-hour examination a large portion of the barium had passed the lesion and at six hours all the barium had passed by except for a trace adhering to the ulcerated area. A diagnosis of malignancy of the jejunum was made.

At operation, a large mass was found overlying the transverse colon. In freeing the growth, an opening was made into an ulcerated section of bowel which was dilated to such an extent that the surgeon believed it to be a portion of the transverse colon. It was found impossible to remove the mass due to the extensive adhesions, therefore a biopsy was taken and the abdomen closed with drainage. The patient died two days following operation.

The autopsy report, as far as it related to the intestine, was as follows: At a point approximately 16 cm. distal to the pylorus the jejunum is dilated to a maximum circumference of 12 cm. The dilated portion measures 15 cm. in length. On section, a firm nodular tumor was disclosed measuring 8×6×5 cm. involving all the layers of the bowel with ulceration of the mucosa. The tumor mass involves further the transverse colon in such a way as to practically encircle it, producing a definite constriction at one point by external pressure. The mucosa of the colon is not involved, but the wall is invaded for a distance of 6 cm. On section the tumor presents a perfectly smooth, gray surface. At the distal end of the balloon-like dilatation of the jejunum, the invasion of the intestinal wall has produced a slight constriction, the circumference at this point measuring only 5 cm. The regional mesenteric glands show extensive involvement

Sections taken through the tumor show highly undifferentiated cells with moderately chromatic, vesicular nuclei and abundant acidophilic cytoplasm. These are growing with no evidence of orderly arrangement, and no suggestion of clumping or alveolar distribution, There is a moderately dense, fibrous tissue stroma. Mitotic figures are quite abundant and there is very little apparent cellular reaction to the tumor. Occasional multinucleated cells are seen, some of which appear to be true giant cells of the foreign body type.

Diagnosis: Malignant tumor, probably primary in the jejunum (leiomyosarcoma or lymphoma) with regional metastases and extension to the colon.

Comment. In this case we have an irregular dilatation of the jejunum corresponding to a large palpable abdominal mass. The irregularity remained fixed and constant at the interval examinations after the motor meal and, although some barium adhered

to the ulcerated surface at the end of six hours, there was no obstruction present. At operation this section of jejunum was so dilated that the surgeon was under the impression that he was dealing with the transverse colon instead of the jejunum.

Case III. A male prisoner at the Norfolk Prison Colony, aged forty-five, was admitted to the hospital because of a right inguinal hernia and a right upper quadrant abdominal mass. The patient complained of recurrent swelling in the right groin after operation for right inguinal hernia, associated with pain and discomfort. He complained also of upper abdominal distress, mild in nature, one or two attacks of vomiting, particularly during the few months before admission. He had almost continual indigestion and flatulence. At the time of admission, however, the patient was comparatively symptom-free, as far as upper abdominal symptoms were concerned. Examination revealed a well-developed, well-nourished white adult male, up and about and in no apparent distress. There was a large swelling in the right groin, definite impulse on coughing, with definitely enlarged inguinal ring. In the right upper quadrant there was a diffuse palpable mass visible on inspection. This mass was non-tender and appeared to be firmly fixed. The heart and lungs were negative.

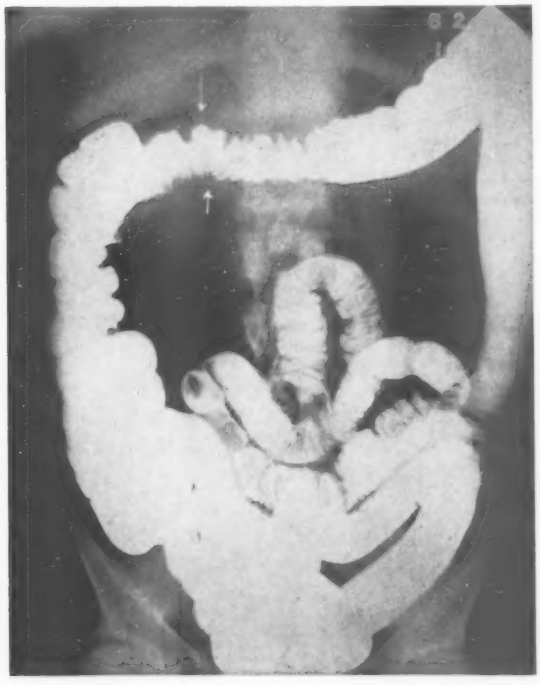

Fig. 4. Case III. The surface of the proximal transverse colon is finely irregular in outline where it is in contact with the large external mass.

Fig. 5. Case III. Showing irregular, ulcerated segment of jejunum within the large soft tissue mass.

Examination of the colon by barium enema demonstrated a pressure defect on the proximal transverse colon produced by the mass, which appeared to be definitely outside the colon (Fig. 4).

Barium administered by mouth showed a normal stomach and duodenum. On the films taken at two, four and six hour intervals, however, an irregular area in the jejunum was demonstrated (Fig. 5). This area measured about 3 inches in length. The wall of the bowel at this point was irregular, the mucosal markings obliterated, the area was rigid, corresponded to the palpable mass and its appearance remained constant on all the films taken. There was no obstruction at this point. In view of these findings a roentgen diagnosis of malignant tumor involving the small bowel was made.

At operation, a large inoperable mass, about the size of a grapefruit was found. It involved the jejunum, mesentery, wall of the stomach, colon, and gallbladder. A biopsy was taken and

Fig. 6. Case iv. Showing ulcerating lesion of the jejunum. Film taken one hour after administration of the motor meal.

the abdomen closed. The patient did poorly following the operation. He developed a foul discharge from the wound, pulse and respirations rose, his condition became progressively worse and he died three days after operation.

The autopsy revealed a large diffuse mass in the mesentery extending to involve all surrounding structures. It had ulcerated into the jejunum and into the colon at the hepatic flexure. Section through the mesenteric end showed increase of connective tissue. At the base of the tumor there were elongated spindle cells with an unusual amount of stroma between. These spindle cells were arranged in palisades and occasionally in pseudo-rosettes. At the top of the peritoneal surface of the tumor mass the tissue was broken down and cells of the chronic inflammatory type were seen.

Diagnosis: Fibrosarcoma of the mesentery of neurogenic origin—either from the sheath of the vagus or from branches of the autonomic system.

Comment. Again we have an irregular segment of jejunum, which in this case is not definitely dilated. The irregular area remains constant on all the films taken during the passage of the barium meal through the small bowel and it corresponds to the palpable abdominal mass. There is no obstruction present, but barium still adheres to the ulcerated surface at six hours. Autopsy demonstrated a sarcoma, probably arising in the mesentery and involving the jejunum and the colon secondarily.

Case iv. A white male, aged sixty-five, entered the hospital because of abdominal pain of seven weeks' duration. For several years the patient had had occasional attacks of acute indigestion characterized by pain in the mid-abdomen relieved by vomiting. Seven weeks before entry, he began to have crampy waves of pain across the mid-abdomen lasting several hours and relieved by catharsis. He was a little more constipated than usual. Five weeks before entry he had a severe grinding pain across the umbilicus followed in a few hours by vomiting which lasted for twenty-four hours. Since that time he had felt hungry all the time but found that a few mouthfuls filled him up and that he vomited very easily. He had lost 20 pounds in weight during the past seven weeks.

Physical examination showed a well-developed, poorly-nourished elderly male. Abdomen slightly protuberant, poorly relaxed. Liver edge felt 1 cm. below the costal border. There was dullness to percussion over an area 6×6 cm. just below and to the right of the umbilicus. The abdominal wall was tense in this region but a mass, the size of a baseball or larger, was thought to be made out.

At barium enema examination the colon filled and emptied normally. It was not displaced or deformed and there was no evidence of intrinsic disease.

After administration of barium by mouth the esophagus, stomach, and duodenum were found to be normal. About 12 inches beyond the duodenojejunal junction however, a grossly irregular segment of jejunum was encountered (Fig. 6). This area was rigid and the appearance remained constant at subsequent examinations after the motor meal. There was no obstruction to the passage of barium, but some barium was found adhering to the lesion at the end of six hours. The roentgen diagnosis was malignancy of the jejunum.

This patient refused operation and entered another hospital some time later. The abdomen

was tapped on two occasions in that hospital and large amounts of clear fluid withdrawn. He still refused operation and died at home a few weeks later.

Comment. Although no operation or autopsy was obtained in this case, the roentgen findings were so characteristic that the diagnosis of malignant tumor of the jejunum seems assured. The subsequent course of the disease is confirmatory evidence. It is interesting that in spite of the history characteristic of partial intestinal obstruction, no obstruction was found to the flow of barium. It is possible that the lesion was at first stenosing and later a wide lumen was formed by necrosis and ulceration within the stenosed area.

Case v. A male, aged forty-two entered the hospital because of attacks of left lower quadrant pain of three months' duration. The pain was a dull dragging ache, lasted two to three hours, and on one occasion was associated with nausea and vomiting. He had never had diarrhea or been constipated. He entered the Portland General Hospital where a diagnosis of malignancy was made and he was referred to this hospital for operation.

Fig. 7. Case v. Plain abdominal roentgenogram showing soft tissue mass within which there is an air-filled cavity.

Fig. 8. Case v. Roentgenogram taken four hours after the motor meal. The soft tissue mass with its air-containing cavity is well visualized. The barium lies in the jejunum and has not yet entered the mass. The barium in the colon is a residue from a previous barium enema.

Physical examination was negative except for a hard, fixed mass in the left side of the abdomen extending from the costal border to below the iliac crest. On rectal examination, a lemon-sized mass was palpable low in the pelvis.

Laboratory Findings: Red blood cells, 5,650,000; white blood cells, 14, 500; hb, 85 per cent. Stool—guaiac test positive on two occasions.

On barium enema examination, the palpable mass was found to be in front of the descending colon and it could not be separated from the colon. There was an oval, air-containing cavity in the center of the palpable mass and, at the lower end, this air-containing cavity showed the mucosal markings of the small bowel.

After administration of barium by mouth, the esophagus, stomach, duodenum and upper jejunum were essentially normal in appearance. At four hours, the barium was about to enter the region of the mass and at six hours, the barium had passed the palpable mass and was

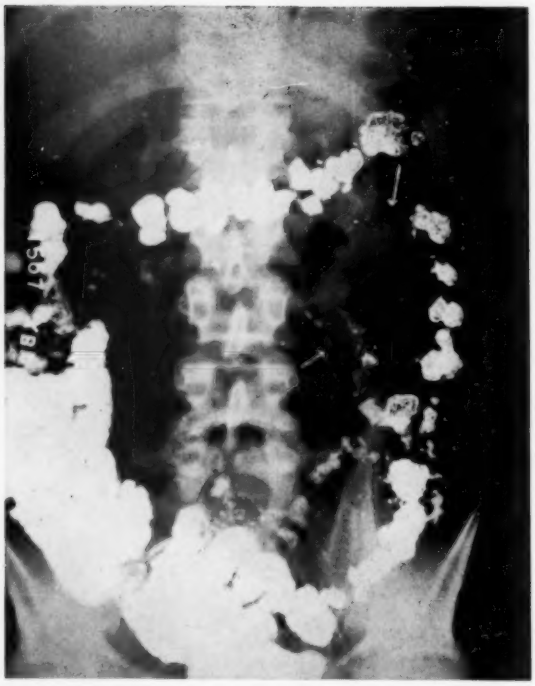

Fig. 9. Case v. Six hour roentgenogram. The barium meal has passed beyond the lesion but there is still barium adhering to the walls of the cavity within the tumor.

almost entirely in the terminal ileum. There was, however, some barium within the mass coating the inside of the irregular gas-containing cavity. There was no evidence of obstruction in the small bowel; in fact there appeared to be hypermotility in the small bowel in the neighborhood of the lesion. The roentgen findings were interpreted as being those of a primary, malignant tumor of the small bowel at about the junction of the jejunum and ileum.

At operation a tumor mass was found surrounding the small bowel which measured 13 cm. in length by 8 cm. in thickness. The tumor had invaded the descending colon and it was necessary to resect a portion of colon as well as the small bowel in order to remove the mass.

The resections were successfully performed and the patient made a good operative recovery. A large retroperitoneal gland, felt at operation, was later treated with deep roentgen therapy and it completely disappeared.

The section of small bowel removed at operation showed a lumen which was grossly dilated within the tumor mass. The dilated portion measured 8.5 cm. in length and presented an irregularly nodular, hemorrhagic surface from which all semblance of mucosa was lost. The wall of the tumor measured 0.7 to 3 cm. in thickness and the tumor had infiltrated the wall of the large bowel without involving the mucosa. The tumor was composed of small, round cells with scanty cytoplasm which resembled immature cells of the lymphocytic series. There were numerous mitotic figures and the cells had a sarcoma-like arrangement. Pathological diagnosis was lymphosarcoma.

Comment. In this case, an abnormal gas shadow, seen on the plain abdominal films, proved to be the dilated lumen of a small bowel tumor. If a film had been taken at five hours when the mass of barium was in the tumor the appearance would undoubtedly have been very similar to that observed in the first four cases.

SUMMARY AND CONCLUSIONS

Malignant tumors of the small bowel are usually stenosing and obstructive. The extraluminal, non-obstructing type, how-

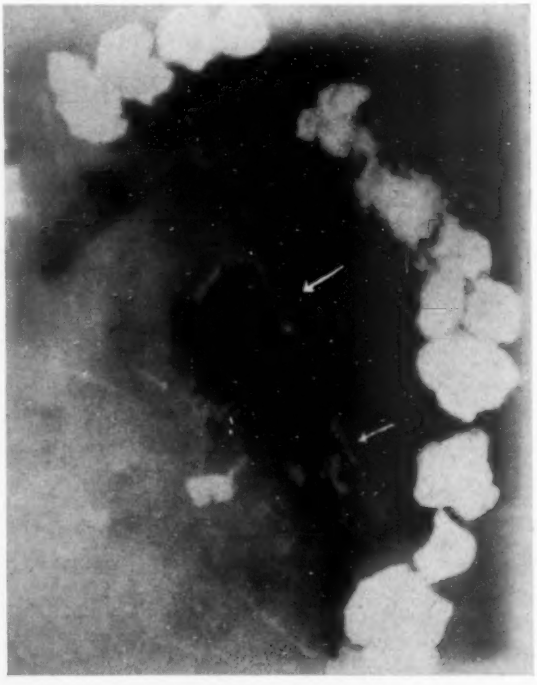

Fig. 10. Case v. Localized film showing barium adhering to the walls of the cavity within the small bowel tumor. Film was taken at six hours after most of the barium meal had passed beyond the lesion.

ever, occurred in approximately 25 per cent of a series of 25 cases observed at the Massachusetts General Hospital. The roentgen findings which were very characteristic were as follows: The involved segment of small bowel was irregular in outline with obliteration of the mucosa and with moderate to marked dilatation throughout the lesion. There was no obstruction but the involved area could be visualized even after the barium column had passed beyond because of a coating of barium adhering to its ulcerated surface. In most of the cases a large mass could be palpated corresponding to the defect in the bowel, this mass often being very large in comparison with the small area of intestine involved.

For the demonstration of these lesions, examination of the small bowel by roentgenoscopy and roentgenography is recommended at two, four and six hour intervals after the motor meal.

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A REVIEW OF SOME FEATURES OF REGIONAL ILEITIS

WITH REPORT OF A CASE INVOLVING APPROXIMATELY THREE FEET OF THE MID-ENTERON

By JOHN SPROULL, M.D.
HAVERHILL, MASSACHUSETTS

IN THIS study it is my intention to review some of the aspects of the disease variously known as terminal ileitis, regional ileitis and chronic cicatrizing enteritis, and also to report a proved case of regional ileitis in the subacute stage. The amount of enteron involved in this case was approximately 3 feet. It was thought, moreover, that the proximal ileum only was involved, although no investigation was conducted which excluded involvement of some part of the distal jejunum. The distal part of the ileum for at least 2 feet proximal to the ileocecal valve was not involved.

It is hoped that the accompanying colored illustrations will prove of educational value regarding the gross pathology of the disease. Not only is the recognition of the histological changes in the affected gut necessary for the ultimate scientific diagnosis by the pathologist, but also a knowledge of the gross pathologic changes occurring in the various stages of the disease is of paramount importance to the roentgenologist and to the surgeon. Since it is a fact that the roentgen appearances are produced almost entirely by the gross pathologic changes, and furthermore since the preoperative diagnosis is almost entirely dependent on correct roentgen examination and interpretation, it is of the utmost importance that the roentgenologist be familiar with the gross pathology of the disease.

The importance to the surgeon of a knowledge of the gross pathologic changes is evident, for only from this knowledge can come his recognition of the disease when the abdomen is opened and the affected intestine visualized; and upon such recognition depends the adequacy of the surgical therapeutics instituted. That a knowledge of the gross pathology of the disease under consideration is not widespread is apparent to me through my personal contact with many surgeons, most of whom have diagnosed the appearances shown in the colored illustrations (Figs. 1 and 2) as those of tuberculosis. Indeed, many otherwise well-informed surgeons, clinicians and roentgenologists, not only in suburban but in metropolitan districts, are totally unfamiliar with the various aspects of the disease regional ileitis.

HISTORICAL

Prior to 1932 there were sporadic reports in the literature of an intestinal condition which resembles the one under consideration and which was called granuloma. Since 1932 considerable literature on the subject has been published, so that at present many reports and articles on granuloma of the intestine are listed.

In 1932 Crohn, Ginzburg and Oppenheimer described a disease of the terminal ileum occurring mostly in young adults and involving 8 to 12 inches of this part of the small intestine. The condition was marked by a characteristic subacute or chronic necrotizing and cicatrizing inflammation, and the authors regarded it as a definite clinical and pathologic entity. In their presentation, which was based on a study of 14 cases observed by them, they discussed in detail the clinical and pathologic features of the disease, and referred briefly to the roentgenologic diagnosis. They stated that the disease is clinically featured by symptoms resembling those of ulcerative colitis, namely, fever, diarrhea

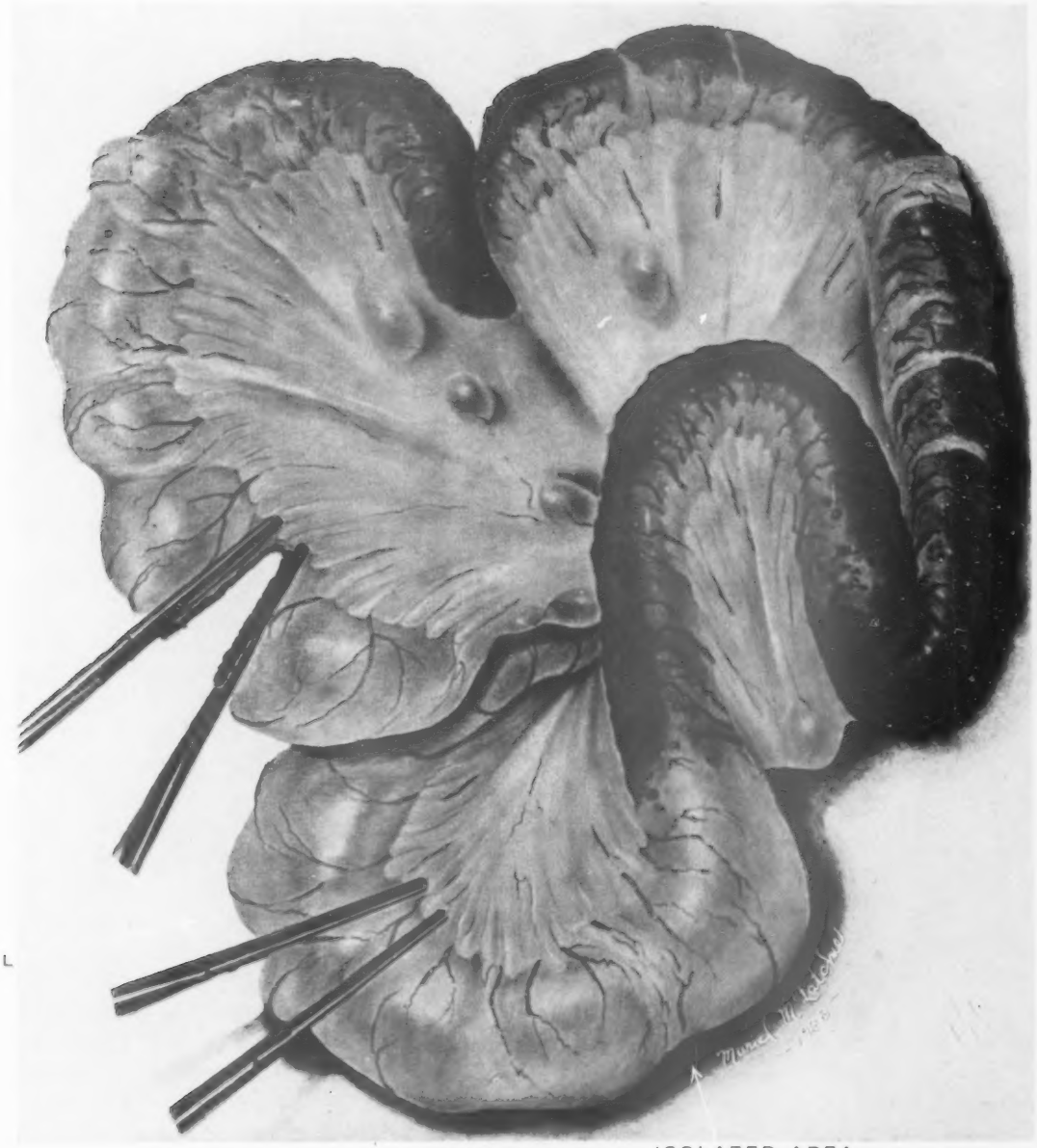

FIG. 1. Appearance of bowel in situ. See text for detailed description.

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and emaciation, leading eventually to an obstruction of the small intestine and to the occurrence of a mass in the right iliac fossa, requiring resection of the involved intestine. They stated very emphatically that the terminal ileum only is involved; that the disease never attacks the large intestine. They said indeed that the proximal surface of the ileocecal valve may be involved, but never the distal side; that the formation of fistulas between the involved loop of the terminal ileum and various segments of the large intestine, or between the involved segment of the ileum and the anterior abdominal wall often occurs; and that the etiology is unknown, the course of the disease relatively benign, and in the cases studied by them all the patients who survived the operative procedures remained well. To this condition the name "regional ileitis" was given.

Later, Harris, Bell and Brunn described a similar pathologic condition involving the jejunum, and in reporting a case suggested the name "chronic cicatrizing enteritis." Still later, Colp described a case with involvement of the terminal ileum and the cecum. This was the first one reported showing simultaneous involvement of the large and small intestine. In January, 1936, Crohn and Rosenak discussed 9 cases of combined ileitis and colitis. In this article Crohn completely reversed his original opinion that the disease involved the terminal ileum only, and stated that the jejunum or ileum may be involved, and that there may be extension from the ileum to the colon, or simultaneous involvement of the ileum and colon. In view of this reversal of attitude on the part of Crohn in regard to the localization of the disease, it is of interest to note that in 1933, when Homans and Hass reported 2 cases of the disease, Homans in a very able discussion questioned the status of the condition known as terminal ileitis as a separate pathological entity. Subsequent contributions have emphasized the accuracy of Homans' observations and deductions.

LOCALIZATION

A study of the literature involving 132 reported cases of granulomata of the intestine has been made. The following table gives the location of each case.

LOCATION OF NONSPECIFIC GRANULOMATA AS SPECIFIED BY AUTHORS

Location	*No. of cases*	
Entire ileum exact 3 proximal feet and 5 distal inches	1	
Ileum alone (exact location not specified)	10	
Jejunum alone	5	
Terminal ileum alone	37	
Terminal ileum, ileocecal valve, and part of cecum	3	
Terminal ileum and ileocecal valve	17	
Terminal ileum and part of cecum	15	
Terminal ileum, cecum, and part of ascending colon	13	
Terminal ileum, ileocecal valve, cecum, and ascending colon	4	
Cecum only	9	
Cecum and ileocecal valve	1	
Cecum, ileocecal valve, and ascending colon	4	
Cecum and ascending colon	5	
Ascending colon	1	
Terminal jejunum and upper ileum (? tuberculosis)	1	(See discussion in text)
Entire small and large intestine	2	(See discussion in text)
Sigmoid only	1	
Transverse colon only	1	
Mid-ileum	1	
Entire colon	1	
Total cases	132	

This study of the localization of granulomata involving the intestinal tract warrants the following statements as representing the present-day concept of this aspect of the disease. The disease may involve any part of the small intestine except the duodenum, or several parts of the same small intestine, for cases have been reported in which areas of considerable length of normal intestine intervened between small or extensive areas of diseased intestine. This latter observation is of the greatest importance, as the treatment at the present time is surgical excision of the diseased intestine, and it is therefore necessary for the surgeon to explore the whole

small intestine so that he may remove all of the involved areas. He must not be content with finding only the one large diseased area. Furthermore, the concept of localization has been extended to include both the colon by direct extension through contiguity of tissue from diseased ileum, and (as reported) isolated areas of colon involved in association with ileal involvement but not dependent on contiguity of tissue; in the latter class of cases some areas in the colon are separated from the diseased ileum by normal intestine. Attention is called to the seeming immunity of the duodenum to the disease under discussion. No proved case of involvement of the duodenum has been found in the literature.

Two items in the foregoing table of localization merit discussion. The first item, "Entire small and large intestine," is based on the report of 2 cases of a pathologic condition entirely similar to regional ileitis as we now know it. These were reported in 1913 by Dalziel who, in describing the process of the disease as involving the whole of the small and large intestine, made no specific reference to the duodenum. He called the condition chronic interstitial enteritis and mentioned its resemblance to tuberculosis. One case was examined post mortem. In the other, the diagnosis was made by exploratory laparotomy, though no part of the bowel was removed for histologic examination.

The unsatisfactory and incomplete nature of the report of these cases furnishes no evidence of duodenal involvement, and as no other reports even suggest involvement of the duodenum, it seems correct to assert that no proved case of duodenal involvement by regional ileitis has been reported.

The second item, "Terminal ileum and jejunum (? tuberculosis)," is derived from a case reported by Schapiro in 1934 in which the disease process involved 2 feet of the distal jejunum and proximal ileum. The pathologic condition in the intestine was perfectly typical of regional ileitis; but at operation some of the enlarged mesenteric lymph nodes were removed and were proved to be tuberculous. These lymph node findings caused some doubt whether the identity of the process in the intestine was ileitis or tuberculosis.

PATHOLOGY

The gross pathologic changes are variable, depending on whether the disease is discovered during the acute, the subacute or the chronic stage. In the acute stage the affected segment or segments of the intestine are red and swollen, with edema of the surrounding tissue and with enlargement of the lymphatic glands of the mesentery.

The gross pathologic changes of the subacute stage, clearly shown in Figures 1 and 2, correspond in most details with the original description of the pathologic manifestations as described by Crohn and his associates.

1. The exterior of the bowel is shown in Figure 1 and attention is called to the following points: (*a*) the roughened granular appearance of the serosa; (*b*) the tubercle-like formation on the serosa; (*c*) the evidences of inflammation as shown by swelling, redness and stiffness of the bowel wall; (*d*) the diminished diameter of the affected segment; (*e*) the varicose condition of the blood supply; (*f*) the edema and inflammation of the mesenteric fat producing a seeming overgrowth of this tissue as evidenced by its extension upon and almost complete encirclement of, the bowel wall (normally the mesenteric fat does not extend beyond the mesenteric border of the small intestine); (*g*) the evident lymph gland hyperplasia. This was much more marked in the original specimen. Indeed, the surgeon found it difficult to avoid incising some of the enlarged glands in resecting the mesentery.

2. The pathologic changes of the interior of the gut are well shown in Figure 2. The items of interest are: (*a*) the abnormal thickness of the bowel wall; (*b*) the row of serpiginous ulcerations extending along the

FIG. 2. Appearance of section of open bowel. See text for detailed description.

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mesenteric border; (*c*) the grayish diphtheritic-like membrane covering the ulcers; (*d*) the islands of isolated swollen mucosa between the ulcers; (*e*) the swollen enlarged appearance of the folds of mucous membrane adjoining the ulcerations (these two latter pseudo-polypoid conditions give rise to the appearances of polyposis seen in the roentgen examination); (*f*) the normal unbroken transverse mucosal folds at one extremity of the section of the gut.

In the chronic stage, the inflammatory ulcerative condition of the bowel is replaced by the development of a condition showing connective tissue proliferation, atrophy of the mucous membrane, and narrowing of the lumen of the bowel. This is the stage most commonly observed by the surgeon, since it is the stage of imperative symptomatology, namely, that of intestinal obstruction.

The histologic pictures show various phases of acute, subacute or chronic inflammation and the presence of giant cells (Figs. 3 and 4).

SYMPTOMATOLOGY

That there is a wide variation in the symptomatology of regional ileitis becomes evident from a study of the published reports of the cases. This variation might well be expected, for just as the gross pathologic picture varies according to the stage at which the disease is discovered, so too will the clinical picture vary.

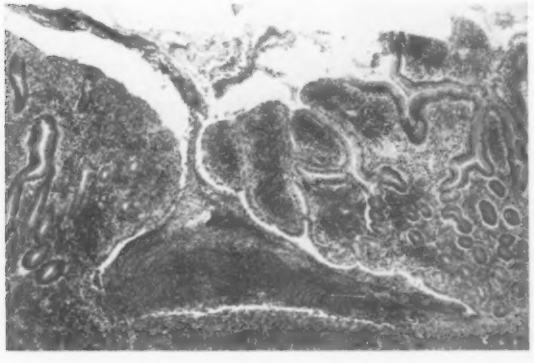

Fig. 3. A section through the mesenteric side of the bowel showing ulceration of the mucosa and a dense inflammatory reaction in the submucosa. Note the marked fibrinopurulent exudate at the base of the crypt.

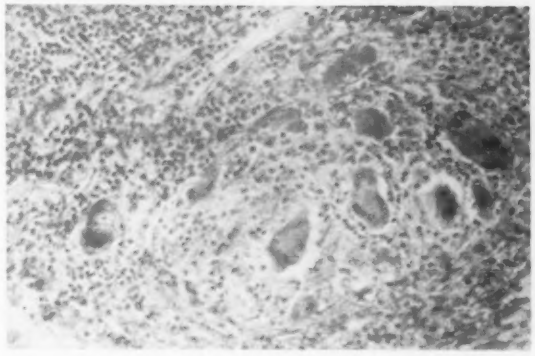

Fig. 4. A section through the submucosa showing multiple giant cells as well as the infiltration of inflammatory cells.

Though it is true that many cases show the clinical picture of ulcerative colitis, namely, fever, diarrhea, emaciation, pus and blood in the stools, it is equally certain that many cases, which at operation show an extensive ulcerative process in the affected segment of small bowel, have but minor subjective or objective symptoms, and in the examination made in the clinical laboratory show little other than the findings of the roentgen examination.

Indeed, the paucity and mildness of the symptoms recorded at the clinical examination, when compared with the severity and extent of the pathologic involvement revealed at operation, is one of the striking features of some cases of the disease. Such a state of affairs noted in a number of the cases in the literature was clearly present in the case reported in this discussion. In this case the only subjective symptoms were attacks of peri-umbilical pain occurring with or soon after the ingestion of food, a loss of appetite and deficiency in energy. The only objective symptoms were the moderate gaseous distention of the abdomen and the clubbing of the fingers. Similarly, the usual positive laboratory findings, other than the roentgen findings, were conspicuous by their absence. A study of the reported cases shows that though many of them exhibit the symptoms of abdominal pain, fever, emaciation, pus and

Fig. 5. Roentgen appearance of subacute stage of regional ileitis. *Note:* (1) the involved area comprising several loops of small intestine; (2) the local stasis. It is unusual to visualize such a length of continuously filled small bowel; (3) the length of the area involved and its high position in the film and its extension transversely suggest rigidity due to inflammatory infiltration; (4) the diminished caliber of the affected segments. Normally the enteron gradually decreases in diameter from the proximal to the distal parts. In this film the involved enteron is narrower than the distal small intestine; (5) the irregularity of the margins of the affected loops of small intestine; (6) the finger-print-depression appearance of the mucosal relief pattern resembling that produced by diffuse polyposis; (7) the absence of dilatation of the loops of small bowel proximal to the involved area. This finding suggests that the local stasis is due to interference with peristaltic activity as the result of inflammatory edema of the bowel wall. The disease has not reached the fibrostenotic stage.

either gross or occult blood in the stools, anemia, leukocytosis, and a palpable mass in some part of the abdomen, a sufficient number of observed cases, presenting only few of these symptoms, justify the conclusion that there exists no typical pathognomonic symptom or group of symptoms of regional ileitis. The larger number of cases at the time of discovery have reached the stage of intermittent, incomplete, intestinal obstruction.

In the case reported here no such symptoms as diarrhea, fever, emaciation, anemia, or pus in the stools were observed. On the contrary, the subject was at times quite markedly constipated, and of ten stools examined for occult blood, eight were negative and two gave only a faintly positive reaction.

The conclusion arrived at is therefore that the only constantly present symptom of regional ileitis is abdominal pain of varying severity in degree, located in any part of the abdomen, but usually peri-umbilical or right sided; this pain is such as may occur in other intra-abdominal diseases, and is not explained by the examination of other viscera. In this reported case, an operation had been performed for an inguinal hernia, which was assumed to be the adequate explanation of the attacks of abdominal pain, and in one case recently seen in consultation, the presumptive diagnosis, before roentgen examination, was gallstones.

The foregoing statements are of importance to the clinician in showing that regional ileitis may occur of considerable severity in degree and with extensive involvement in amount, and yet the clinical laboratory findings other than those of the roentgen examination may be practically negative.

ROENTGENOLOGY

The roentgen findings in regional ileitis vary with the stage of the disease at which the examination is made, and attention is again called to the importance of a basic knowledge on the part of the roentgenologist of the gross pathologic changes present in the various stages of the disease. These pathologic structural alterations are entirely responsible for the variations from the normal condition seen in the roentgen examination, and without a knowledge of these alterations correct interpretation of the roentgen findings cannot be made.

In the acute stage of the disease the diagnosis of appendicitis is usually made, and at this period roentgen examinations are uncommon. A knowledge of the pathologic changes present at this time suggests that the variations from the normal likely to be found in the roentgen examination would be similar in kind to those of the subacute stage, but of lesser degree.

In the subacute stage, the roentgen findings in the affected segment or segments are moderate narrowing of the lumen of the bowel, irregularity of the margins of the bowel, some degree of local stasis, rigidity of the bowel wall, and a mucosal relief pattern of the finger-print-depression type resembling that produced by polyposis. These findings are well shown in Figure 5. The roentgenologic appearances of the later stage (commonly called the fibrostenotic stage), as described by Kantor, consist of the following when applied to the terminal ileum, where this stage is most commonly seen: (1) a filling defect of varying length in the terminal ileum; (2) dilatation of the loops of ileum proximal to the lesion and the presence of puddling and fluid levels in this area; (3) abnormality in contour of the last filled loop of ileum; (4) the presence of a string-like shadow of barium, of varying length, which represents the area involved and which Kantor calls the string sign (Fig. 6).

The string sign does not always show the extent of the area involved. In some cases the fibrostenotic changes are limited to a comparatively small area of the diseased intestine. In such circumstances the string sign will show the extent of the fibrostenotic area while the remainder of the involved intestine will present the roentgen findings characteristic of the subacute stage. Such conditions were present in the case represented by Figure 6. Here the fibrostenotic process was limited to the terminal 3 inches of the ileum, while the remainder of the involved area showed the findings of the subacute stage of the disease. Where the colon is involved, the barium enema is valuable and may reveal

Fig. 6. The following should be noted: (1) the fibrostenotic area of diseased ileum immediately proximal to the cecum. Kantor's string sign is present; (2) the area of subacute ulceration presenting the mucosal relief pattern suggestive of polyposis. In other films this part of the intestine when filled showed moderate diminution of the diameter of the bowel lumen. Kantor's string sign was absent in this area; (3) the dilated normal bowel, the result of intermittent incomplete obstruction.

characteristic filling defects, abnormal mucosal relief pattern, or fistulous tracts between the small and large intestine.

DIFFERENTIAL DIAGNOSIS

It is apparent that the differential diagnosis must include all other diseases with intra-abdominal pain as a symptom, especially such diseases as have symptoms suggestive of involvement of the small or large intestine. The three most important diseases to be differentiated are appendicitis, ileocecal tuberculosis and ulcerative colitis. It seems likely that, until the profession shall maintain an attitude of awareness of the possibility of ileitis as a simulant of acute appendicitis, the diagnosis of this group of ileitis cases will not be made ex-

cept by exploratory operation. So many subjective and objective phenomena are common to both diseases that the diagnosis of the one or the other has proved very difficult.

The use of the barium enema in a case where the diagnosis was not clear might prove an aid. It has been shown in the case of many, if not of most, individuals that the ileocecal valve is incompetent during the administration of a barium enema. This incompetence permits the filling with barium of a considerable part of the terminal ileum, the area of ileum usually involved in the cases of regional ileitis which simulate appendicitis. The demonstration by this method of examination of a filling defect involving a considerable part of the terminal ileum would favor the diagnosis of ileitis rather than of appendicitis.

The discovery that regional ileitis may involve the large intestine, by or without direct contiguity of tissue, has multiplied the difficulties in the differential diagnosis from ileocecal tuberculosis. I am, however, impressed with the statement of Crohn and his associates, that in ten years, only 3 proved cases of ileocecal tuberculosis have been observed at the Mt. Sinai Hospital in New York, though during that period many cases of ileitis have been diagnosed and treated as ileocecal tuberculosis. I have knowledge of similar mistakes occurring in other hospitals, and the conclusion must be made that, granting the existence of a lesion involving the terminal ileum and cecum, there is a statistical preponderance of incidence in favor of ileitis.

In the consideration of the differential diagnosis of ulcerative colitis and ileitis, one readily observes the similarity of the various phases of the two diseases, and it may yet be found that there is an etiologic factor common to both conditions. It is well known that ulcerative colitis makes its initial appearance low down in the colon, and it is recognized that extension of the disease process may take place from the proximal colon to the ileum. Those familiar with the gross pathologic appearances of the interior of the gut in ulcerative colitis will readily note the similarity in appearance of the interior of the enteron when regional ileitis is present to that of the colon in cases of ulcerative colitis.

In the absence of fistulous communication between the small intestine and the sigmoid, visualization of the typical ulcerations of ulcerative colitis in the rectum and sigmoid is the most important factor in the differential diagnosis of ulcerative colitis and ileitis. In those cases which have fistulous communication between the diseased ileum and the sigmoid there may be extension of the ulcerative process from the former into the latter; and with such conditions obtaining, the discovery of ulcerations in the rectum would not have the same significance as where fistulous communication was absent.

The roentgen examination with the barium enema may reveal findings suggesting ulcerative colitis, but such findings have not now the same significance in differentiating ulcerative colitis from ileitis as when the latter disease was supposed to involve the small intestine exclusively. For these reasons, the value of careful visual search for the typical ulcerations of ulcerative colitis in the rectum can hardly be overemphasized, yet even with the knowledge derived from all these methods of examination, considerable difficulty may still be experienced in differentiating the group of diseases which presents simultaneous involvement of the terminal ileum and colon, and it is likely that in some cases exploratory operation will be necessary to establish the identity of the pathologic process present.

CASE HISTORY

J. H., Hebrew, male, aged fourteen, seen December 12, 1935, complained of attacks of peri-umbilical and epigastric pain. The attacks had occurred irregularly for the past three years, but for the past six months have been present daily either during the ingestion or soon after the ingestion of every meal. The duration of each attack of pain was about an hour and usually the pain was of such severity as to compel the patient to leave the table and lie

down. The attacks of pain, however, had never been of such duration as to prevent attendance at school, nor had they interfered with normal sleep.

His guardians reported that the boy was listless and showed no inclination to participate in the usual games and sports common to lads of his age. There had been a definite loss of appetite. There had been no nausea or vomiting and no alterations of bowel habits except occasional constipation.

The history of previous illness was not important, except for a right inguinal hernia for which herniotomy had been performed two and one-half years before. This operation was undertaken for the relief of abdominal pains, similar in character to those present during the past three years.

Physical examination showed a somewhat stunted boy with some pallor especially marked about the nostrils and the skin surrounding the mouth; but the mucous membranes appeared of normal color. His weight was 88 lb. There was no emaciation. The examination of the heart and lungs showed no evidence of disease in these organs. The abdomen was moderately distended, but no evidence of ascites was present. The spleen and liver were not palpable and there was no tenderness, spasm or mass detected in the abdomen. The rectal examination was negative except for a small fissure; the blood pressure was 110/60; the urine was clear and showed no albumin, sugar, pus or blood. The nose, throat and teeth were negative, and the reflexes on the extremities were normal. There was no palpable gland enlargement. The temperature at 3 P.M. was 99° F. The serological test for syphilis was negative. The blood examination showed no anemia or leukocytosis and the smear was normal. There was marked clubbing of the fingers of both hands, and of ten stools examined for occult blood, eight were negative and two slightly positive.

Diagnosis in abeyance. Advice, roentgen examination of the chest, renal tract and gastrointestinal tract.

Roentgen report. Renal tract and chest negative. Gastrointestinal tract: Normal esophagus, stomach, duodenum and colon.

At the six hour examination a definite abnormality involving a large section of the mid-enteron was noted. This area, thought to involve 30 to 40 cm. of bowel, showed six hour stasis, narrowing of the lumen and irregularity of the margins of the gut, and a mucosal relief pattern suggesting polyposis. The involved area appeared stiff and rigid, and although it extended throughout more than one loop, no angulation was present. There was no dilatation of the loops of the small intestine proximal to the involved area (Fig. 5). A diagnosis of an inflammatory ulcerative lesion of the proximal ileum was made and re-examination was advised.

The roentgen examination was repeated but in a varied manner from the first. The patient was given his barium meal at home at 8:30 A.M. and reported one hour later at the roentgen department for his first film. Subsequently films were taken every half hour for five and one-half hours. The abnormality of the small bowel found at the first examination was verified, but also a rather unusual condition was noted in that on the film taken one hour after the ingestion of the barium meal, the head of the barium column was well advanced in the cecum, in spite of the fact that the boy was constipated. In other words, the patient had small bowel diarrhea, with large bowel constipation. Operation was advised and the advice was accepted.

A laparotomy was done on January 23, 1936, by Dr. Leland McKittrick of Boston. At the operation an inflammatory ulcerative condition was found involving approximately 3 feet of the mid-enteron. All of the diseased intestine was continuous, with the exception of one isolated area, separated from the main area of intestinal involvement by about 5 inches of normal intestine. The lymphatic glands of the mesentery were markedly enlarged, and in situ the gut presented the appearance shown in Figure 1. There was no free fluid in the peritoneal cavity. The diseased portions of the small intestine, and parts of the normal intestine at each extremity of the involved gut with the adjoining mesentery, were excised. An end to end anastomosis of the cut ends of the small intestine was performed, and the abdomen was closed without drainage.

The patient made an excellent recovery from the operation, the wound healed by first intention, and he was discharged from the hospital on February 25, 1936. His weight at the time of discharge from the hospital was 81 lb.

Following discharge from the hospital, the patient made satisfactory progress.

On April 11, 1936, roentgen examination showed no evidence of small bowel pathology present.

Final clinical examination was made on June 3, 1936, three months subsequent to his discharge from the hospital, and at this time the patient weighed 100½ lb., a gain of 19½ lb. since the date of leaving the hospital, and he presented the appearance of perfect health. His guardians stated that the boy's appetite was excellent, his disinclination to play was gone, and he had had no return of abdominal pain since his recovery from the operative procedures. A complete physical examination showed no evidence of disease.

The following is the pathology report made by Dr. Tracy B. Mallory, of the Massachusetts General Hospital on January 23, 1936.

ILEUM

Gross: A resected portion of ileum 79 cm. in length. The mesentery is thickened and firm and it contains several enlarged soft grayish red lymph nodes measuring up to 1.2 cm. in diameter. The muscle wall is thickened, firm and fibrous, measuring from 3 to 5 mm. The upper portion of the mucosa for a distance of 6 cm. shows normal red smooth surface with folds of mucosa in parallel arrangement. A sharp line of demarcation presents, below which the mucosa is pale, irregular and arranged in nodules measuring 3 to 6 mm. in diameter which are separated by bands of fibrous tissue. In areas measuring up to 5 mm. in diameter the mucosa is lost and the surface here is gray, firm and hemorrhagic and definitely ulcerated.

Microscopic: Examination shows a severe grade of enteritis with both acute and chronic features. As the gross examination indicated, there is a rather characteristic variation in the picture on different sides of the gut. On the wall opposite the mesenteric attachment, the mucosa is free from ulceration, but swollen, edematous and moderately infiltrated with eosinophiles, lymphocytes and plasma cells. The lymphatics are markedly dilated in both mucosa and submucosa. Numerous lymphoid follicles are present, often with active germinal centers, and all stages of their formation can be traced. As the lateral walls of the bowel are reached, the inflammatory infiltration becomes denser in all layers of the bowel wall and small ulcers begin to appear deep in the crypts between the villi. At the bases of these, defects in the epithelium appear and a fibrinopurulent exudate is being poured forth. On the mesenteric side of the wall the changes reach their maximum. Large areas of ulceration with complete loss of epithelium and a diphtheritic membranous exudate are encountered. These overlie a greatly thickened submucosa densely infiltrated with plasma cells and less numerous eosinophiles. In places the ulceration extends almost down to the muscularis. The inflammatory infiltration involves both layers of the muscularis and extends outward focally into the mesentery. Lymphatic dilatation which is everywhere obvious in mucosa and submucosa stops short at the muscular rings. The pentrating blood vessels, however, show a marked inflammatory thickening of their adventitia.

In all layers of the wall, mucosa, submucosa, muscularis and serosa, focal areas of a different type of inflammatory response are seen. These consist of single or multiple giant cells indistinguishable from the Langhans type, accompanied by varying numbers of large mononuclear phagocytes. No foreign bodies or inclusions can be made out though vacuoles are occasionally present. They do not contain lipoid. These aggregates occasionally strongly suggest tubercles and a Ziehl-Nielsen stain done with a positive control fails to bring out an acid-fast bacillus. An occasional giant cell is seen in the acute inflammatory exudate covering the mucosal ulcerations. A few of these focal areas are found well out in the mesentery. There is nothing in any of the sections to suggest the evidence of present or past fistulous tracts and it is felt that such an explanation for the giant cell foci can be ruled out. Gram stains of the gut fail to show any organisms except an occasional one on the luminal surface. One section shows a serosal lymphatic completely plugged with large mononuclears showing a foamy lipoid-filled cytoplasm. The mesenteric nodes show only nonspecific hyperplasia.

Diagnosis: Regional ileitis.

COMMENTS AND CONCLUSIONS

(1) Crohn and his associates merit great commendation for their work in relation to this disease. Their writings are masterpieces of accurate observations, logical deductions and meticulous recordings.

(2) The incidence of the disease here discussed is increasing, and its geographical distribution is widening, as evidenced by published reports of proved cases from all parts of this country and some parts of Europe.

(3) Because of its variability in symptomatology and of lack of pathognomonic clinical manifestations, the recognition of regional ileitis before surgical exploration is dependent largely on roentgen examination.

(4) The importance of a knowledge of the gross pathology of the various stages

of the disease is emphasized. Such knowledge is necessary for a correct understanding of the roentgenologic manifestations of the disease and for the application of proper surgical therapeusis.

(5) The case herein reported shows the need for detailed roentgenologic study of the small bowel in all cases of abdominal pain of uncertain origin. The modus operandi of roentgenologic study of the small bowel has not yet become standardized. Frequent observations covering a period of six hours following the ingestion of the barium meal has seemed satisfactory.

(6) The recognition by roentgenologic methods of such an obscure case as herein recorded evidences the great aid that roentgenology contributes in the diagnosis of internal diseases; and nowhere has it attained a higher degree of excellency than in the diagnosis of diseases of the gastrointestinal tract. The younger generation takes the rôle roentgenology plays in the diagnosis of disease as a matter of course. But those of the older generation well know how it has replaced doubt with certainty and indefiniteness with accuracy, and all should acknowledge their gratitude to Roentgen and to all other scientific workers who have made this state of affairs possible.

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ROENTGENOLOGICAL MANIFESTATIONS OF CARCINOMA OF THE COLON

By ROY G. GILES, A.B., M.D., F.A.C.R.
TEMPLE, TEXAS

THE diagnosis of the more common diseases of the colon is ordinarily not difficult if one follows the recognized procedure of a careful history, physical examination and proctoscopic examination of the rectum and sigmoid. In addition, the stool should be carefully searched for pus, blood and parasites. Finally, a thorough roentgen examination should be made.

The opaque enema study and its various refinements give the most comprehensive information as to the presence and extent of organic lesions, as well as the presence and extent of anomalies and functional disorders of the colon.

All organic lesions of the large intestine produce changes in the wall of the intestine, and the roentgenoscopic observation of the opaque enema should be studied on the screen from the time the enema enters the rectum until the filling of the cecum is completed. In order to detect abnormalities which may later be hidden by an overlying loop of normal bowel, rotation of the patient during the administration of the barium enema to obtain different angles is indispensable.

The roentgenologist should be familiar with the normal variations of the colon and should recognize the following: (1) changing defects produced by gas in the colon or by air injected with the opaque enema; (2) pressure from bone, as in the case of the sigmoid flexure, where it crosses the superior pelvic strait; (3) localized deformities and narrowing produced by spasm.

Extrinsic lesion should be excluded. Occasionally a large fecalith may give rise to obstruction or produce a filling defect, with a corresponding mass, and the sign complex wrongly be attributed to a new growth.

Appendicial abscess should be recognized from the history of recent pain, the leukocyte count, and the integrity of the cecum roentgenographically.

When all the foregoing factors can be dismissed from consideration, filling defects, obstructions, and other abnormal manifestations are to be regarded as indicative of intrinsic disease.

Deformities produced by localized areas of chronic ulcerative colitis, tuberculous colitis, diverticulosis and benign polypi must be distinguished roentgenologically from carcinoma of the colon by the fact that they are usually too extensive to be due to carcinoma, which, if it were as extensive, would be diagnosed from ascites, marked cachexia and palpable metastatic lesions. The roentgenographic appearance of ulcerative colitis is never one of obstruction except from cicatricial strictures. The roentgenological changes in the contour of the colon are recognized as a blurring of the normal distinct outline of the wall of the large intestine and a narrow, tube-like colon with absence of haustra.

Tuberculous colitis affects the cecum and ascending colon. Cecal tuberculous colitis is suggested roentgenographically by poor visualization and hyperirritability of the cecum. Pulmonary tuberculosis, accompanied by a history of colonic symptoms, usually pain and intermittent diarrhea, is suggestive of tuberculous colitis.

Diverticula are usually best seen in the film taken after evacuation of the enema and in that taken after insufflation with air. In some cases the diverticula do not fill when the enema is used; in others barium remains in the diverticula for days or weeks.

Complete obstruction may be produced by an inflammatory mass caused by diverticulitis and may necessitate the same pro-

cedures for relief of obstruction as those which would be required if the lesion were malignant.

Polypi tend to be multiple and should be suspected in all cases of rectal bleeding. The patient appears well, having few or no other symptoms. The intestine should be completely emptied of all fecal material when searching for polypi in the upper colon. The polypi are best demonstrated by finger-like areas in the colon filled with barium. The double contrast enema will outline the lesions with a faint ring of barium in the air-filled lumen of the colon.

The roentgenological signs of carcinoma of the colon can be elicited when the disease manifests itself clinically by ulceration and obstruction. Generally the roentgen appearance goes hand in hand with the symptoms. The more severe the symptoms, the more obvious are the roentgen appearances; and, occasionally when subjective and objective evidence from other sources is lacking or very indefinite, the roentgenologist may discover an entirely unsuspected intestinal neoplasm.

The three roentgenographic criteria in the diagnosis of malignant lesions of the colon are: (1) obstruction; (2) stricture; (3) irregular contour.

Obstruction is observed on the fluoroscopic screen when the progress of the barium is retarded. The lumen of the intestine remains closed in spite of the continued pressure by the head of the barium column. The closed lumen is not relieved by changing the position of the patient or by palpation of the colon.

A stricture of the colon at any point that remains as a constant narrowing, unrelaxed by persistent manipulation or the insufflation of air after the barium has been expelled, is almost certain to be due to a malignant lesion.

Gross irregularity of outline is easily distinguished from the normal outline, but at times one is confronted with an early lesion producing only a slight deviation from the normal contour of the colon. A deviation though slight, that is persistent, accompanied by spasm or interference with peristalsis, is reasonably suspicious of carcinoma of the colon.

The two special procedures for diagnosis of carcinoma of the colon are proctoscopic and roentgenological examinations. With the proctoscopic examination, lesions of the rectum which have been palpated by digital examination can be visualized by careful roentgen examination and their exact nature and extent determined. A thorough roentgen examination will frequently demmonstrate neoplasms lying above the palpating finger. In certain cases, such as diverticulosis and polyposis, examination after partial evacuation of the enema may be informative. The "double contrast" method of distending the colon with air may be of value in demonstrating lesions which would be concealed by the complete barium enema and occasionally serves best to bring out the anatomical characteristics of the deformity produced by carcinoma of the colon.

The basic and cardinal roentgenological procedure of investigating the colon is visual, reinforced by manipulation of the diseased parts. A film will often provide information which was not so clearly available at the roentgenoscopic examination.

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THE USE OF THORIUM DIOXIDE IN THE ROENTGENOGRAPHIC STUDY OF LIVER ABSCESS*

By ROBERT J. REEVES, M.D.
DURHAM, NORTH CAROLINA

DURING the past five years, there has appeared in the literature, a number of articles on the use of colloidal thorium dioxide in roentgenological diagnosis. Three years ago, we[1] gave a preliminary report on the use of colloidal thorium dioxide (thorotrast) in the diagnosis of liver abscess. A résumé of the literature was made and the dangers, indications, and contraindications were given. The tissue changes following the administration of these colloidal thorium preparations have been well described. The preparation has been used rather extensively in clinical medicine, but is still considered by the Council on Pharmacy and Chemistry of the American Medical Association[2] as unsafe for general clinical use, as insufficient time has elapsed to determine the ultimate changes in the liver and spleen. This preparation has been widely used in the study of malignancy, where the chief concern is the detection of liver metastases. The spleen and lymphatic system in cases of myelogenous and lymphatic leukemia have been studied as to the therapeutic action of thorium dioxide (thorotrast) both as a primary agent and also secondary in conjunction with roentgen therapy.

In the study of liver abscess by the aid of thorium dioxide, we are able to visualize the abscess cavity on the roentgenogram, due to the fact that after the usual doses, the reticulo-endothelial cells, chiefly the Kupffer cells, of the liver and the large polygonal cells of the spleen by absorbing the thorium are made more dense, whereas the content of the abscess cavity, not taking the thorium, is contrasted as an area of diminished density. We are then able to accurately localize the cavity by means of roentgenograms, and the surgeon determines the nearest point of approach without the possibility of producing peritonitis.

In many instances, liver abscess is unsuspected or cannot be localized until roentgenograms of the chest and abdomen are made, showing an elevated right diaphragm and depressed lower liver margin. This is especially true in amebic infection, where the abscess is often symptomless. On the flat roentgenograms, the cavity cannot be demonstrated due to the fact that the density of the fluid in it is the same as the surrounding liver tissue. A differential diagnosis must be made to rule out other causes of hepatitis. Careful stool examinations, of course, are routine where amebiasis is suspected.

TECHNIQUE

Thorium dioxide is put up in ampules containing 12.5 c.c. in colloidal suspension. The contents of six ampules, or 75 c.c. of the colloidal suspension, are added to 100 c.c. of physiological salt solution and given intravenously by means of a regular infusion set. If there is any suggestion of a possible reaction, two ampules are given daily for three successive days. The reticulo-endothelial cells concentrate the thorium rapidly and on the third day following the last injection, stereoroentgenograms of the liver region are made. More films are made a few days later to study the rate of concentration.

POSSIBLE DANGERS

The Council on Pharmacy and Chemistry of the American Medical Association has considered thorium dioxide as unsafe for routine clinical use. Stewart, Einhorn and Illick,[4] in 1931, found there was suffi-

* From the Roentgen-Ray Department, Duke University Hospital.

Fig. 1. Case 1. Five days after the injection of 75 c.c. of thorium dioxide. Numerous small areas of diminished density can be seen.

cient radioactivity to fog a photographic film after twenty-four hours. By means of the gamma-ray detector, we have been able to detect as much as 80 per cent increase in radioactivity over normal atmospheric conditions, such as cosmic rays. This would indicate that the drug is more radioactive than we formerly believed. It is therefore administered only in cases where the differential diagnosis is most obscure. The drug has also been recently used in arteriography and ventriculography.[5] The fact that it diffuses with the spinal fluid is very helpful in the study of the fourth ventricle and the cerebral aqueduct. The same dangers apply here, however, as elsewhere in the body.

CASE REPORTS

Case 1. A colored male, aged forty-two, was admitted to Duke Hospital, February 13, 1936, complaining of pain in the abdomen of eighteen months' duration. He had been in good health until August, 1934, when he was seized with an acute pain in the abdomen, accompanied by nausea and vomiting. The pain localized in the right upper abdomen. The stools at this time were dark brown. The attacks recurred every seven to ten weeks, and the last was accompanied by chills and fever, occurring five days before admission.

At the time of admission, the temperature was 101° F., and the white blood count was 10,400 with 78 per cent polymorphonuclear leukocytes. A clinical diagnosis of appendicial abscess, with a possible subdiaphragmatic abscess, was made. Roentgenograms of the chest and abdomen disclosed an elevated, irregular right diaphragm and hepatic enlargement. The chills and fever became more frequent. Repeated blood cultures were negative.

One week after admission, 75 c.c. of thorium dioxide suspension was given intravenously. A roentgenogram of the abdomen five days later disclosed a moderately enlarged liver, with several areas of diminished density, varying in size from 2 to 6 cm. in diameter (Fig. 1). Because of the findings, the abdomen was explored. The liver was found to be enlarged and within it, several areas of softening could be detected. Packs were placed against the surface of the liver. The patient's condition became steadily worse, and he died on March 10.

The necropsy disclosed an organized appendicial abscess and many small abscesses throughout the liver. The portal system was filled with many thrombi, and the portal vein, just at its entrance to the liver, was filled with

Fig. 2. Case 1. Cross section of the liver showing extensive infection of the portal vein.

thick yellow pus (Fig. 2). A smear made of this fluid showed a number of various sorts of organisms, both gram-positive and gram-negative.

Case II. A white girl, aged nineteen, was admitted to the Hospital complaining of pain in the abdomen and vomiting of five weeks' duration. Her present illness started in April, 1935, following operation for ruptured appendix. Following operation drainage was profuse for several weeks. After being discharged from the hospital, she had several chills and attacks of vomiting. Two weeks prior to the second admission, she began running a spiking temperature and vomited continually. Physical examination disclosed a dehydrated girl, apparently quite ill. The right side of the abdomen was spastic and tender to palpation. The sinus tract was draining thick creamy pus. Smear disclosed a mixed infection of *B. coli* and *Staphylococcus aureus*.

Lipiodol was injected and the sinus tract was demonstrated as far as the hepatic margin. After running a stormy course, on August 1 she was given 75 c.c. thorium dioxide suspension intravenously. A roentgen examination

Fig. 3. Case III. Six days after the injection of thorium dioxide. Liver greatly enlarged and an area of necrosis involving the greater portion of the liver.

Fig. 4. Case III. The colon filled with barium appeared normal, but was pushed down by the enlarged liver.

one week later disclosed a central abscess of the liver, measuring 10 cm. in diameter. A rib resection was performed and the abscess opened and drained. The abscess continued to drain and on October 20 the patient was discharged, much improved.

Case III. A white woman, aged seventy-eight, was admitted to the Hospital, August 30, 1934, complaining of weakness, indigestion, and gradual loss of weight of one year's duration. She had been well until one year previously when she was seized with a sharp pain in the right abdomen. A mass appeared in the right upper quadrant, and for six weeks there was intermittent pain, nausea, and vomiting. Since this attack, she had grown progressively weaker until the time of admission, when she was confined to bed.

Physical examination disclosed a large, soft mass in the right upper quadrant, extending beneath the costal margin. The blood and urine examinations were negative, except for a marked secondary anemia. Roentgen examination of the gallbladder and gastrointestinal tract were negative, except for the liver which appeared to be greatly enlarged.

A study of the liver was made by means of thorium dioxide, 75 c.c. of the suspension in-

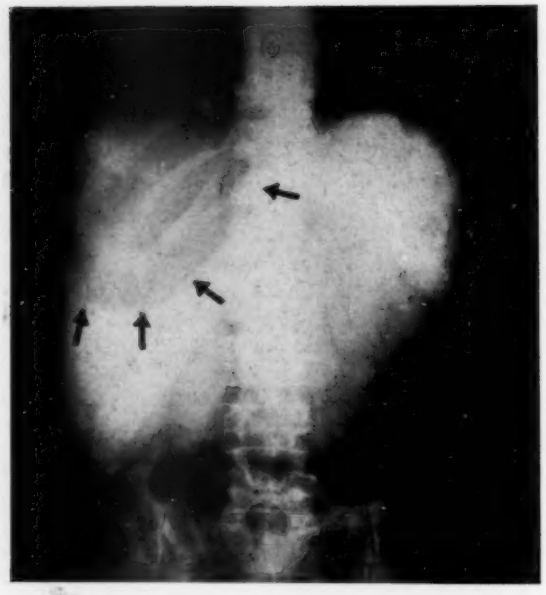

Fig. 5. Case III. After aspiration of 2.5 liters of fluid.

jected intravenously on September 10. Roentgenograms six days after injection disclosed a huge liver abscess involving the upper two-thirds of the liver (Figs. 3 and 4).

On September 19, the abdomen was opened and the abscess drained, about 2.5 liters of a slightly clouded fluid being obtained (Fig. 5). Cultures of this fluid and study of the walls of the abscess disclosed no organisms. The opening in the cavity was brought up and sutured to the peritoneal opening. The abdomen was closed without drainage. Recovery was uneventful and the patient appears well today.

Case IV. A colored male, aged twenty-four, was admitted August 27, 1934, complaining of a stab wound in the abdomen. An exploratory operation was performed and a stab wound about 1 inch in length was found in the stomach. There was also a small wound in the outer margin of the liver. These areas were closed and abdomen closed without drainage.

Five days after admission, lobar pneumonia developed in the right lower lobe. Twenty-six days after admission, a roentgenogram showed the pneumonic process in the lungs to have cleared up, but the right diaphragm was elevated and there was a continuous elevation of temperature. Conditions continued unchanged, and on November 27, 75 c.c. of thorium dioxide suspension was given and an abscess visualized in the posterior aspect of the liver. The abscess was drained and hemolytic streptococci were obtained. Recovery was uneventful and the patient has remained well.

Case V. A colored male, aged twenty-eight, was admitted to Duke Hospital, April 15, 1935, complaining of pain in the abdomen of four months' duration. He had been in good health until December, 1934, when he was seized with a sharp cramp-like pain, radiating to the lower abdomen. A clinical diagnosis of appendicitis was made and the treatment was conservative. This attack lasted about six weeks, gradually subsiding and he returned to work. After four weeks, he had a second attack, accompanied by nausea and vomiting, chills and fever. The impression was that there had been a ruptured appendix with subsequent subdiaphragmatic abscess. During this time, he had lost about 45 pounds in weight.

The accessory findings were as follows: Urine and stools negative. The white blood count showed 11,900 cells, 85 per cent being polymorphonuclear leukocytes. There was a daily spiking temperature reaching 103° F. A roentgenogram of the chest disclosed a high fixed right diaphragm.

On April 17, 60 c.c. of thorium dioxide sus-

Fig. 6. Case IV. Large area of diminished density along the lateral margin of the liver.

pension was given intravenously and a roentgenogram of the liver five days later disclosed a large abscess in the right lobe of the liver, measuring 14 cm. in diameter. The abdomen was opened, the peritoneum packed against the liver, and four days later the abscess was drained, about a liter of foul smelling pus being obtained. A culture, however, failed to show any organisms. The recovery was uneventful and the patient at the present time is clinically well.

Case vi. A white male, aged fifty-one, was admitted to the Medical Service, November 21, 1932, complaining of pain below the right costal margin and diarrhea for seven weeks. Five years before entry, the patient began having bimonthly attacks of diarrhea, and, occasionally, blood and mucus-streaked stools. These attacks were mild and produced no great discomfort until seven weeks before entry, when the pain became much more severe. The diarrhea was worse at this time. Stool examination disclosed many motile amebae. A roentgenogram of the chest disclosed a highly elevated right diaphragm and enlarged liver. These findings were suggestive of liver abscess, and 72 c.c. of thorium dioxide suspension injected intravenously. Roentgenograms disclosed a large abscess cavity which measured 14 cm. in diameter (Fig. 7). The cavity was aspirated and 1,500 c.c. of thick yellow pus was obtained No organisms could be cultured.

The patient was placed on anti-amebic regimen and three years later appears clinically well.

SUMMARY

Thorium dioxide has now been in clinical use for about ten years, and in our experience seven years. Our patients still living have shown no ill effects from its use.

It is definitely known, however, that thorium and its associated decay products do emit small quantities of high energy radiation of voltage comparable to that of gamma rays from radium. Whether or not the cumulative intensity is sufficient to be biologically injurious has not yet been ascertained.

In our experience, the drug is never given except in cases of malignancy or where the differential diagnosis is obscure and the prognosis grave.

Fig. 7. Case vi. Abscess cavity well visualized.

CONCLUSIONS

Because of the above physical findings and insufficient time period, we consider the use of thorium dioxide dangerous and do not advocate its use except in those cases having a grave prognosis, such as malignancy with metastases in the liver or liver abscess which cannot be localized clinically.

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ROENTGEN PELVIMETRY

A STUDY OF 325 CONSECUTIVE, UNSELECTED PRIMIPARAE WITH COMPLETE CLINICAL FOLLOW-UP*

By HERBERT A. JUDSON, M.D.
LOS ANGELES, CALIFORNIA

THE records of the ante partum roentgen examinations of 325 consecutive unselected primiparous patients have been studied and compared with their clinical and delivery records for the purpose (1) of comparing the pelvic measurements as obtained by the roentgen examination with those obtained by external pelvimetry; at the same time, to place on record other pertinent data brought out by the study, and (2) of discovering, if possible, any relationship between the size and shape of the pelvis and of the fetal head as determined by the roentgen examination and the type of labor encountered. To what extent, if any, may the roentgen findings anticipate the course of labor in any given case?

The method of examination used is that of stereoroentgenography, as described by Johnson.[1] This has been found to be a simple procedure and convenient for the patient. That it is accurate has been repeatedly proved by measurements of dried pelves, and by checking with measurements of heads of infants delivered by cesarean section or in breech deliveries where there has been no molding.

Routinely, three diameters of the inlet are measured: the conjugate vera and right and left obliques; two of the outlet: the posterior sagittal and bis-ischial; two of the fetal head: the occipitofrontal and suboccipitobregmatic. Other diameters are added as may be indicated in special cases. Recently the films were reviewed and the transverse diameter of the inlet measured and made a part of the data.

Table 1 gives the average, minimum and maximum diameters of the group.

There were 7 (2 per cent) with a conjugate vera of 10.5 cm. or smaller; 33 (10 per cent) between 10.6 and 11.5 cm.; 101 (31 per cent) between 11.6 and 12.5 cm.; 117 (36 per cent) between 12.6 and 13.5 cm.; and 67 (21 per cent) above 13.5 cm. This prevailing large size is perhaps accounted for by the class of patients in the group, they being all of the white race and from the so-called middle or white collar classes. There was likewise a noticeable absence of definite pelvic deformities or abnormalities. One pelvis could be classed as justominor; the others fall within the limits of fairly frequent anatomical variations.

TABLE I

AVERAGE, MINIMUM AND MAXIMUM DIAMETERS

	Average (cm.)	Minimum (cm.)	Maximum (cm.)
Inlet			
C.V.	12.6	9.3	15.0
R.O.	13.3	11.0	15.8
L.O.	13.4	11.6	16.5
Inlet index (Sum of C.V., R.O. and L.O.)	39.7	32.8	45.8
Transverse	13.9	11.5	16.5
Outlet			
P.S.	7.0	4.4	9.8
B.I.	11.6	9.0	14.8
Outlet index (Sum of P.S. and B.I.)	18.6	15.8	23.8
Fetal head			
O.F.	10.9	9.4	12.6
S.B.	9.2	8.2	10.9
External pelvimetry			
I.S.	24.9	20.0	31.5
I.C.	28.2	21.5	33.5
E.C.	19.8	16.5	24.0
R.O.	22.1	19.0	32.0
P.S.	7.5	5.0	10.0
B.I.	10.0	7.0	12.0
Outlet index	17.5	14.0	22.0

The diameters of the fetal head are somewhat smaller than the average normal at

* The material presented is from the obstetrical service of Dr. Allen Ross of the Ross-Loos Medical Group, Los Angeles, California.

term, due to the roentgen examination being made from a few days to three to four weeks before labor. It is estimated that the fetal head grows at the rate of 1 cm. in diameter in the last four weeks. Allowance was made on this basis, or in special cases, re-examination for the diameters of the fetal head was made at the onset of labor. In 18 per cent of the cases with vertex presentation movement of the fetal head prevented its accurate measurement; 2.8 per cent of the cases were in breech presentation where a second examination to include the fetal head was made if deemed advisable; 97.2 per cent of the cases were in cephalic presentation.

Measurements of the pelvic inlet as obtained by roentgen and external pelvimetry were compared, with results as shown in the following table.

TABLE II

COMPARING EXTERNAL CONJUGATE AND CONJUGATE VERA DIAMETERS

External conjugate of	19 cm.	19.5 cm.	20 cm.
Number of cases	29	34	38
Corresponding conjugate vera	10.5 to 14.7 cm.	9.3 to 14.0 cm.	10.2 to 14.6 cm.
Variation	4.2 cm.	4.7 cm.	4.4 cm.

There were 31 cases with a conjugate vera of 11.8 to 12 cm. In these, corresponding external conjugates measured from 17 to 24 cm., a variation of 7 cm.

In comparing measurements of the outlet, there were 138 cases with a bis-ischial of 10 cm. as obtained by external pelvimetry. Of these the roentgen bis-ischial was

Smaller by	2 mm. in		2 cases or	1.5%
Same			2	1.5%
Larger by	1 mm. to 1 cm. in		34 cases or	25.0%
	1 cm.	2 cm.	62	45.0%
	2	3	26	19.0%
	3	4	10	0.7%
	4	5	2	1.5%

There is the same approximate degree of variation as in the inlet, but here the roentgen measurements are almost without exception larger than the manual, as might be expected from the intervening soft tissue encountered in the manual method. It should be noted that the clinical measurements of the outlet are read directly from the Thoms pelvimeter without allowance by addition to the bis-ischial or subtraction for the posterior sagittal.

Comparing the posterior sagittal, there were 35 cases measuring 7.5 cm. by external pelvimetry. Of these, the roentgen posterior sagittal diameter was

Larger by 1 mm. to 1 cm. in 6 cases or 17%
Same in 3 cases or 8.5%
Smaller by 1 mm. to 2 cm. in 26 cases or 74%

Thus, the roentgen posterior sagittal diameter was the same or smaller in 82.5 per cent of the cases.

Considering the outlet index, 300 cases were compared, as follows:

Roentgen smaller by	4 to 5 cm. in	1 case or	0.33%
	3 to 4	0	
	2 to 3	3	1%
	1 to 2	17	6%
	0 to 1	50	17%
Total		71	24%
Roentgen same as clinical in		22 cases or	7%
Roentgen larger by	0 to 1 cm.	69	23%
	1 to 2	75	25%
	2 to 3	40	13%
	3 to 4	17	6%
	4 to 5	6	2%
Total		207	69%

Here the degree of variation is about the same again as in the inlet, but the roentgen measurements are the same or larger in 76 per cent of the cases.

It is thus seen how unreliable and misleading external pelvimetry is in the estimates of diameters of the relatively normal pelvis, particularly of the inlet. In the outlet the discrepancy is not so marked, but there is a definite tendency to underestimate in the clinical measurements. In borderline cases or in the abnormal or deformed pelvis where accurate measurements are particularly needed, it is impos-

sible to obtain them by other method than the roentgen examination. No accurate determination of the size of the fetal head can be made except by the roentgen method.

Attempted correlation between the size and shape of the pelvis and of the fetal head with the course of labor was next undertaken. The conjugate vera being the most important single diameter of the inlet, its relation to the course of labor was studied. There were 19 cases with a conjugate vera of 11 cm. or less; of these 11 (or 57 per cent) had definite difficulty in labor, requiring operative intervention. This is distinctly higher than the 23 per cent dystocia found for the entire group.

The relation of the outlet to labor was considered, first in a comparison of the posterior sagittal diameter. There were 22 cases where this diameter measured 5.5 cm. or less. Of these 2 (or 10 per cent) had difficult labor.

There were 10 cases with a bis-ischial of 10 cm. or less; of these 2 (or 20 per cent) had difficult labor. The outlet index is perhaps of more importance than either posterior sagittal or bis-ischial alone. There were 25 cases with an outlet index of 17 cm. or below. Of these 6 (or 24 per cent) had dystocia.

From this study of diameters it would appear that labor increases in difficulty where the conjugate vera is short, particularly below 11 cm. Very little dystocia was encountered which could be attributed to the outlet. There were no definite funnel pelves, where the bis-ischial measures below 8 cm. or the outlet index below 15 cm.

There were 8 patients (2.5 per cent) delivered by cesarean section. Of these 1 had a definitely justominor pelvis, and another was a borderline case. Of the remaining 6, section was performed for other reason than that of cephalopelvic disproportion, 2 patients being for pre-eclamptic toxemia, 2 for cervical dystocia, 1 for a large uterine fibroid obstructing the outlet, 1 an elderly primipara with a rather small pelvis and large infant.

TABLE III

	Cases	Percentage
Female or Ovoid Type (Transverse diameter 1 cm. or more larger than anteroposterior)		
Total	156	50 (Thoms: 51.8%)
Large (A.P. over 12 cm.)	98	31
Average (10.5 to 12 cm.)	55	18
Small (under 10.5 cm.)	3	1
Round Type (Transverse less than 1 cm. larger than anteroposterior)		
Total	109	34 (Thoms: 35.5%)
Large (A.P. 13 cm. or over)	65	20
Average (A.P. 11 to 13 cm.)	44	14
Small (A.P. under 11 cm.)	0	0
Anthropoid Type (Transverse diameter less than anteroposterior)		
Total	54	17 (Thoms: 12.6%)
Large (A.P. 14 cm. or over)	25	8
Average (A.P. 11.5 to 14 cm.)	29	9

There has been an increasing tendency to place more emphasis upon the shape of the pelvis than upon its size or measurements. The cases in this series were therefore tabulated according to the outline suggested by Thoms[2] with the figures shown in Table III. It will be seen that the types of pelves encountered follow fairly closely the figures given by Thoms.

Considerable importance has also been given to a posterior position of the fetal head as being a frequent cause of difficult labor. This is borne out in the present series, where 61 per cent of the dystocia cases in the entire group were in the transverse or posterior positions. We found 103 (or 34 per cent) of the cephalic presentations to enter labor in the posterior position. Of these cases, 49 (or 48 per cent) were of the ovoid type; 37 (or 36 per cent) were of the round type; 18 (or 17 per cent) were of the anthropoid type, paralleling so closely the average types for the entire group that it is difficult to attribute this posterior position to any particular shape of pelvis.

It was also found that approximately the same proportion of these posterior cases occurred in the different sizes of pelves as obtained for the entire group. Therefore, it was not found possible to attribute this posterior position to any particular size of pelvis.

Recently, efforts have been made to estimate the weight of the fetus from roentgen measurements of its head, notably by Ball and Marchbanks,[3] with a cephalometer, and by Clifford[4] with a weight chart based on the length of the occipitofrontal diameter. Of the patients in the present series where the roentgen examination had been made within fourteen days of the time of delivery and where there had been no movement of the fetal head, there were 7 with an occipitofrontal diameter of 10.5 cm. The birth weight of these 7 infants varied from 5 lb. 1 oz. to 8 lb. 1 oz., with an average weight of 6 lb. 9 oz. Of 8 infants with an occipitofrontal diameter of 11 cm., birth weight varied from 7 lb. 5 oz. to 8 lb. 6 oz., with an average of 7 lb. 13 oz. There were 6 with an occipitofrontal diameter of 11.5 cm. whose birth weight varied from 6 lb. 4 oz. to 8 lb. 3 oz., or an average of 7 lb. 7 oz. There were 3 with an occipitofrontal diameter of 12 cm. whose weight was from 7 lb. 1 oz. to 7 lb. 12 oz., average 7 lb. 4 oz., and 1 with an occipitofrontal diameter of 12.2 cm., weight 6 lb. 6 oz., another with an occipitofrontal diameter of 12.6 cm., weight 6 lb., 11 oz. Because of these discrepancies it has not been deemed feasible to make weight estimations, dependence being placed upon accurate diameters of the size of the fetal head.

CONCLUSIONS

(1) Accurate roentgen measurements of the internal diameters of the pelvis bear but little relation to the clinical measurements commonly taken.

(2) Contracted or abnormal pelves are relatively rare, being found in only about 0.3 per cent in this series. Thus, it would seem that the clinical diagnosis of cephalopelvic disproportion as an indication for cesarean section is made much more frequently than it actually occurs.

(3) Posterior positions are frequently associated with dystocia. The cause for this condition has not been demonstrated in the present study, it apparently bearing but little relationship to the size and shape of the pelvis in this series.

(4) While in many cases it may be possible to estimate roughly the weight of the fetus from the length of its occipitofrontal diameter, discrepancies occur frequently enough to render such estimates unreliable.

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THE ROENTGENOGRAPHIC DIAGNOSIS OF SOFT TISSUE TUMORS EXCLUDING THE BREAST

By JOHN R. CARTY, M.D.
NEW YORK CITY

THE roentgenographic study of soft tissue tumors often gives valuable and sometimes decisive information. While soft tissue tumors, particularly those in the extremities, are accessible to palpation, biopsy, etc., nevertheless, it is our opinion that no study of a soft tissue tumor is complete without a careful roentgenographic survey. An excellent illustration of this was brought to our attention recently in 2 instances where a diagnosis of lipoma was made and excision attempted without a roentgenographic study. In each case, a severe hemorrhage was encountered and what appeared to be a simple procedure eventually necessitated a second extensive operation for a deep-seated hemangioma.

FIG. 1. A diffuse lipoma of the arm. Air has been injected between the superficial fascia and the muscle. The fascia has pushed away from the muscle showing no evidence of invasion by the tumor.

It must be stressed that in order to obtain any measure of success a careful soft tissue technique must be employed. We have discussed this at length in a recent article. In addition, the roentgenologist should have a thorough knowledge of the anatomy of the soft parts, particularly in relation to the respective shadows seen on the roentgenogram. This can readily be acquired by making fasciagrams of the cadaver and then dissecting the part, using the fasciagram as a control. The shadows can be identified with a minimum of effort. Without this knowledge, the complexity of the shadows is apt to confuse the observer, leading to erroneous conclusions.

The tumors commonly encountered in the soft parts may be divided into benign and malignant groups. In this paper we will omit a consideration of the purely skin tumors, such as basal cell carcinoma, etc., as in most of these cases roentgenography does not yield much of value. In the benign group, lipoma, fibroma, neurofibroma, hemangioma, lymphangioma, and myoma are the most common.

There is a group of conditions which give rise to tumor-like masses but are not, strictly speaking, tumors; in this group we include ganglion, foreign body reactions, aneurysm, arteriovenous aneurysm and calcification of hemorrhagic exudates in muscle and other tissues.

The malignant tumors may be divided into two groups. The primary group includes fibrosarcoma, liposarcoma and myosarcoma. In the secondary group of tumors, there are those that invade the soft tissues by direct extension or by metastases from a primary source elsewhere. Fibroperiosteal sarcoma, osteogenic sarcoma and Ewing's tumor of the bone often are seen in the soft tissues by direct extension.

There are seven important points which

should be determined, if possible, in every roentgenographic study of a tumor:

(*a*) *Point of Origin.* At times it may be difficult to determine from what anatomical structure the tumor arises. It is logical to assume that in many instances the tumor arises from a structure in which, or in the neighborhood of which, it has its greatest mass. Thus, if a primary tumor is noted in the subcutaneous reticulated structure, it probably arises from tissue in that structure. However, this cannot always be determined. Injection of air directly into the tissue surrounding a tumor may be of great help in outlining the latter and showing any possible point of attachment. This is more successfully accomplished if a tumor lies in the panniculus in a region where the latter is loose with a relatively small amount of fibrous strands. Thus, in the region of the heel and the lateral thigh, difficulty would be encountered in distributing the air.

(*b*) *Character of the Tumor Itself.* One should note whether or not the tumor is represented by an area of increased or decreased density. The character of the density should be noted, particularly whether or not there is mottling or trabeculation.

(*c*) *Encapsulation.* It should be noted whether the tumor is diffuse or localized. If it is localized, it should be noted whether or not there is a capsule. The integrity of a capsule becomes a matter of great importance in determining whether or not a process is malignant; generally speaking, if the tumor breaks through the capsule, it is malignant. Unfortunately, however, not all encapsulated tumors which have not broken through are benign.

Fig. 2. Note the extreme distention of the neck and face tissues by air accidentally introduced following pneumothorax. The right parotid gland can be seen distinctly. The best results are obtained in air contrast methods with soft tissue tumors in localities where the tissues are loose.

Fig. 3. Tumors caused by arteriovenous aneurysm. This somewhat resembles a hemangioma. The vessels composing the tumor are larger. In our experience calcium deposits are rare. One mass is seen in the palm between the second and third metacarpals. The other is adjacent to the outer margin of the radius.

(*d*) *Invasive Properties.* Particular attention should be paid to ascertaining whether or not a tumor has extended beyond its point of origin. In determining this, fasciagraphy is of great help and at times may be the only positive way to determine this point. Figure 1 shows a huge diffuse lipoma of the arm. We were unable to determine from the plain roentgenogram whether or not the tumor extended beyond the superficial fascia into the muscle. This was an important point in deciding whether

an attempt should be made to remove the huge mass. Air was injected under the superficial fascia and it was seen to be pushed away from the muscles. The morphology of the latter appeared normal. Subsequent operation confirmed our findings.

(*e*) *Multiplicity*. One should note whether the tumor is single or multiple.

(*f*) *Calcium*. The presence or absence of calcium should be noted. If calcium is present it is usually deposited in one of three distinct forms: (1) stippling, (2) circular areas commonly seen as phleboliths, (3) extensive flat reticulated masses.

By following this outline no essential fact in establishing the diagnosis should be omitted. It also serves to help the observer in evaluating the important anatomical features.

Lipomas may arise anywhere but are most frequently seen in the panniculus. They usually appear as areas of slightly increased density, although occasionally one is seen which appears as a faint area of decreased density that may be diffused or encapsulated. The diffuse lipomas often appear as an accentuation of the normal anatomy of the subcutaneous reticulated structure, i.e., it is wider, the vertical reticulations are thicker and more numerous. The small localized tumors are apt to be amorphous. The larger ones are generally mottled, depending on the amount of fibrous tissue present. They do not break through the capsule and do not invade beyond the point of origin although they may cause adjacent pressure; they may be single or multiple and do not show calcium deposits. Liposarcoma is rare and has a tendency to invade. It is similar to lipoma except that it is invasive and the ones we have encountered have considerable fibrous strands.

Fibroma may arise from fibrous tissue throughout the soft parts. There may be diffuse fibrosis but usually the tumor is localized and may be encapsulated—they are areas of slight density with a definite trabeculated appearance but rarely quite amorphous. They do not invade and usually do not lay down calcium. Neurofibroma generally has the same characteristics except there is usually less trabeculation and the tumor may be multiple. The tumor is apt to be in the deeper structures in the neighborhood of a large nerve.

Neurofibrosarcoma has the same characteristics except for its invasive tendencies.

Hemangioma may arise anywhere. There are two types, the most common being the diffuse type but occasionally one sees an encapsulated tumor. They are perhaps the most characteristic of all the soft tissue tumors, there being numerous small worm-like shadows of slightly increased density with enlarged vessels leading to the tumor. If encapsulated, it usually does not break through but it may extend beyond the point of origin, particularly along vascular channels. Calcification is very frequent in these tumors and is an important differential point. Calcium deposits are circular with a small core of decreased density.

Lymphangioma may be superficial or deep. The tumor is usually not encapsulated. Dilated lymph channels are seen as poorly defined linear shadows of increased density. Often these have a vertical direction. Sometimes one notices an increase in density of the fibrous reticulations of the panniculus if the tumor is located there. Calcium is not commonly seen.

Chronic lymphatic obstruction (elephantiasis) gives a striking roentgenographic appearance. The panniculus is enormously widened. The muscle mass is correspondingly decreased in size. Enormous vertical striations of fibrous strands are seen running from the skin to the superficial fascia.

Arteriovenous aneurysm may resemble the diffuse type of hemangioma. However, the worm-like shadows are much larger and the vessels running into the mass are usually larger.

True aneurysms are most frequently seen in the popliteal regions or the axilla. They are deep-seated, oval or round amorphous encapsulated shadows of moderately increased density. They push surrounding

structures and often faint calcific shadows are seen in the walls. In most instances, the artery can be traced into or from the mass. The outlines are apt to be somewhat blurred.

Myoma is usually a deep-seated tumor rising in the muscle structure and is difficult to differentiate from fibroma. Sometimes calcification is seen of the flat reticulated type.

Myosarcoma is invasive but otherwise the same as myoma.

Soft tissue roentgenography may be of great help in differentiating between fibroperiosteal sarcoma and osteogenic sarcoma. Besides the well-known appearances of the osseous structures in osteogenic sarcoma, we frequently note a fine stippling of calcium in the periphery of the tumor mass. This is lost with the usual technique. In addition, the familiar fine ray-like calcium deposits close to the bone become visible sooner.

Calcification in hemorrhagic exudate is sometimes confused with osteogenic sarcoma. The calcification is of the flat reticulated type. The ray formation is not present. There is no evidence of the fine stippling seen in osteogenic sarcoma.

A ganglion shows as a well-defined faint amorphous circular tumor having relation to linear tendon shadows. They are frequently seen about the wrist or ankle.

Foreign body tumors are often seen following the injection of paraffin about the face or about the site of injection of irritating substances. They are generally local tumor-like masses with surrounding fibrosis. The roentgen findings in paraffinoma are somewhat disappointing when compared with the physical findings. Irregular amorphous shadows of but slightly increased density, these may be surrounded by a reticulated zone of fibrous tissue forming a sort of capsule.

CONCLUSIONS

(1) Roentgenographic study of soft tissue tumors often gives valuable information to the clinician.

(2) The important features to be noted are enumerated.

(3) The use of air injection in their diagnosis is briefly discussed.

(4) Roentgenographic appearances of the various soft tissue tumors are discussed at length.

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MULTIPLE CALCIFICATIONS IN THE OVARY

(PSAMMOMA OF THE OVARY)

By N. W. LOUD, M.D.
NEW BRITAIN, CONNECTICUT

CALCIFIC deposits are of fairly frequent occurrence in the various organs and systems of the body. Multiple calcifications or psammomata are frequently reported in the brain or meninges or in connection with various portions of the central nervous system. Some calcium is found in most gallstones, and it is the chief constituent of the calculi of the genitourinary system. Calcareous deposits are frequent following atheromatous changes in blood vessel walls.

The occurrence of multiple calcifications in the ovary, however, does not appear to be so frequent; at least comparatively few reports of this condition are found in the literature. Ewing[2] describes psammoma and psammo-carcinoma and an illustration is given of an "adeno-carcinoma of the ovary with abundant calcification concretions—psammoma." In the text of his description[3] of papillary scirrhous adenocarcinoma of the ovary, he states, "calcification granules formed about the capillaries in the stroma or in the epithelial masses may be a very prominent feature, psammocarcinoma. The formation of these granules is preceded by colloid degeneration."

Koch[4] in 1911 considered the occurrence of calcification in the female genital organs of special significance. He says, "They may be looked upon as characteristic and pathognomonic of a certain type of tumor, for instance, the ovarian cystoma. Under certain conditions the calcification in the female sexual system may be of such an extent that one may be justified in speaking of the calcification of an entire organ complex as in 'lithopedia,' calcified placenta, or calcification in uterine myomata." In the ovary, "deposits of calcium concretions are nearly always found in papillary ovarian cystomata; similarly, they are found in a considerable number of cases of ovarian carcinomata, especially in carcinomata derived from papillary ovarian cystomata." Koch concludes: "Psammoma bodies or corpora aranacea, which must be strictly differentiated from corpora amylacea, and in contrast to the latter always develop on a basis of hyaline degeneration, are found outside the central nervous system, very frequently in association with affections of the female genital system, most frequently in inflamed or neoplastically changed ovaries."

REPORT OF CASE

White female, aged forty-seven, was admitted to the New Britain General Hospital October 7, 1935, for abdominal complaint and pelvic disturbance. The past history was essentially negative except for the fact that she had had the left kidney removed twenty-nine years before in another city, a definite report of which was not obtainable, but she thought the diagnosis was tuberculosis, and does not know whether this was confirmed by pathological examination of the kidney after its removal. She was operated on at the New Britain General Hospital, October 11, 1935, by Dr. George W. Dunn and a large right ovarian tumor removed which proved to be a multilocular papillary cystadenoma of the ovary, approximately 7.5 cm. in diameter. Two small fibromyomata were enucleated from the uterus also at this time, and an abscess was drained which obscured the posterior cul-de-sac and the left side of the pelvis, so that the left ovary was not seen or examined at the operation. The patient made a fairly good postoperative recovery, except that drainage continued from the pelvic region, with the formation of a sinus. This sinus continued draining slightly through the following winter and spring, and was demonstrated by lipiodol injection on June 3, 1936 (Fig. 1). In this film a mottled shadow was shown in the left pelvis in addition to the lipiodol within the sinus tract. The character of the mottling and the shape and position of the group of shadows suggest multiple calcifications in the left ovary.

In order to prove that these shadows were not produced by a group of lipiodol droplets, or possible calculi in a diverticulum from the bladder, the lipiodol was withdrawn, and the patient given a period of several weeks for complete drainage of the lipiodol residue. Examination was then made July 10, 1936, with the bladder injected with air by Dr. Roger Scully. The lipiodol was found to have entirely vanished from the sinus, and the mottled shadow previously seen in the left pelvis even more sharply delineated, and apparently having no connection with the bladder (Fig. 2).*

Fig. 1. June 3, 1936. Lipiodol injection of sinus to pelvic cul-de-sac. Mottled oval shadow discovered in left pelvis believed to be produced by psammoma of the left ovary.

From the operative report and discussion with the surgeon, we feel that pedunculated fibroids with multiple calcifications can be eliminated as a source of the shadow in the left pelvis, since he removed such fibroids as were present and removable at time of operation in October, 1935. A few months would be too short a time for a new fibroid to develop and certainly too short for it to develop calcification.

Sections of another case of the adenocarcinoma type of psammoma were examined

* After very kindly examining the films in this case and reviewing the clinical and surgical data, Dr. John D. Camp of the Mayo Clinic stated that the appearance was similar to other cases which he had seen of multiple calcifications in the ovary. We wish to thank Dr. Camp for checking this report for us, and Dr. Stewart for his examination of our slides.

Fig. 2. July 10, 1936. Mottled shadow persisting after complete drainage of lipiodol and injection of air into the bladder—eliminating possible group of calculi in diverticulum of the bladder.

under the microscope, and the calcareous concretions within the lumina of the anaplastic

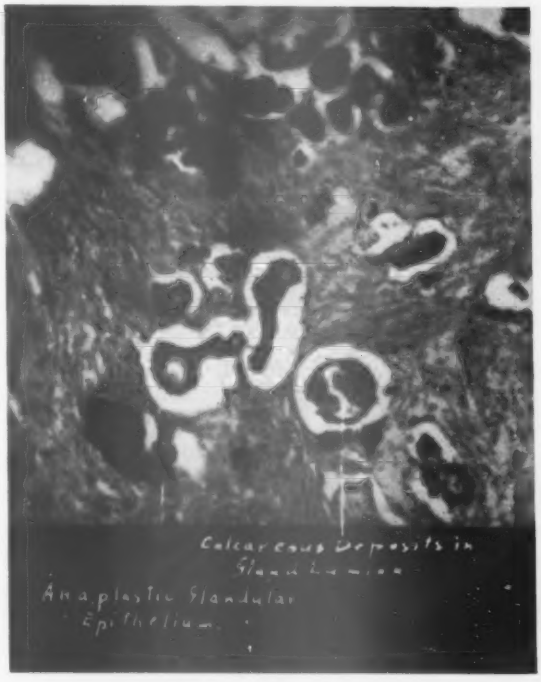

Fig. 3. Photomicrograph showing calcareous concretions in gland lumina in metastatic psammocarcinoma (×400).

glands can be seen in Figure 3. In this case, the biopsy was obtained from the mesentery in the abdomen, there being multiple metastases and so much matting with adhesions that the pelvic organs could not be examined. The sections, however, were sent to Dr. Ewing's laboratory, and Dr. Stewart expressed his opinion that there were evidences of adenocarcinoma with psammoma bodies apparently arising from the ovary, thus giving some substantiation to our conclusions.

SUMMARY

Multiple calcifications in the ovary are associated occasionally with multilocular cystadenoma and adenocarcinoma of the ovary, being then designated as psammoma or psammo-carcinoma of the ovary. A case is presented giving roentgenological evidence of this condition.

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RADIATION TREATMENT OF CARCINOMA OF THE BUCCAL CAVITY

By RICHARD DRESSER, M.D.
BOSTON, MASSACHUSETTS

and

CHARLES E. DUMAS, M.D.
WORCESTER, MASSACHUSETTS

DURING the past five years great advances have been made in radiation therapy. This is particularly true in the treatment of carcinoma of the mouth. Many cases in the so-called "inoperable" group which were formerly considered hopeless are now being cured by radiation, and a large number are obtaining very satisfactory palliation. It is the purpose of this paper to set forth in some detail the technique which we have developed for the irradiation of carcinoma of the tongue, tonsil and buccal mucosa.

The natural course of carcinoma of the mouth is extremely variable. Lesions on the anterior portion of the tongue, the mucosa of the cheeks, and the hard palate are, in general, clinically much less malignant than lesions on the posterior part of the tongue and tonsil. Carcinoma in the anterior part of the mouth may remain localized for a considerable period of time, and it is here that intensive interstitial irradiation or wide surgical excision will accomplish the most brilliant results. Carcinoma in the posterior part of the mouth usually metastasizes early, and local irradiation or surgical excision will rarely control the disease unless accompanied by dissection or irradiation of the cervical lymph nodes.

Although in some clinics the treatment of carcinoma of the mouth has become entirely a radiological problem, it is our belief that a small, well-localized lesion, particularly in the anterior part of the mouth, can, in most instances, best be handled by surgical excision. Such lesions, of course, respond very well to adequate doses of radium or roentgen rays, but surgery is quicker and generally causes the patient less discomfort. Unfortunately, only a small proportion of cases fall in this favorable group, and the radiologist is called upon to cope with the great majority of neoplasms of the buccal cavity.

Little is known regarding the cause of carcinoma of the mouth. The long-continued use of tobacco with the formation of areas of leukoplakia which subsequently undergo malignant degeneration undoubtedly plays a part in some cases. The chronic irritation from the sharp edge of a carious tooth or a poorly fitting denture seems to be a factor in the production of some cases of carcinoma of the tongue. A diffuse hopeless type of carcinoma of the tongue is frequently seen in association with syphilis.

The early symptoms are usually a small lump or ulceration which may be noticed by the patient or frequently is discovered by the patient's dentist. Occasionally the primary lesion goes unnoticed and enlargement of the cervical lymph nodes from metastases first brings the patient to a physician. A slight persistent soreness of the throat may be the first symptom of an extensive carcinoma of the tonsil or base of the tongue.

The clinical diagnosis of carcinoma of the mouth usually presents no difficulty to one who is familiar with this condition, but certain inflammatory processes may give rise to confusion. The great importance of a biopsy on all suspicious lesions of the mouth should be strongly emphasized, for early diagnosis is of paramount importance. Biopsy should also be done in the clinically obvious cases. The pathological grading according to the degree of malignancy is of some help in predicting the radiosensitivity of the growth, but does not help much in the prognosis as to radio-

curability; that is, a high grade malignancy may show a satisfactory immediate response to a moderate dose of radium or roentgen rays, whereas a more differentiated type of growth usually requires a much larger dose to obtain regression. In either case a better prognosis as to the final outcome can be made from the size and anatomical location of the lesion than is possible from the histological examination alone.

Having established the diagnosis, one is confronted with the problem of treatment. This can best be discussed under two headings: first, the treatment of the local lesion; second, the treatment of the cervical lymph nodes.

The patient, unless edentulous, should at once be referred to the dentist. All teeth presenting extensive caries should be extracted and the others should be thoroughly cleaned. It will be pointed out later that the extraction of teeth, even some months or years after heavy irradiation, is a dangerous procedure. If the local lesion is small and there is no clinical involvement of the cervical lymph nodes, one of four methods of local treatment should be carried out: the implantation of gold or platinum radon "seeds"; the implantation of radium element needles; the intraoral application of filtered radium by means of molds; direct intraoral treatment by high voltage roentgen rays.

If radon seeds are employed, they should be distributed as evenly as possible throughout the lesion slightly less than 1 centimeter apart. It is our practice to use seeds of 1 millicurie strength. In the process of decay, each seed will deliver a total of 132 mc-hr. It is rarely advisable to deliver total dosages higher than 1,800 mc-hr., which means a maximum of about fifteen seeds. If this figure is exceeded a prolonged period of radiation slough may ensue. Radium seeds possess the advantage of being easily applied; in fact, they may be used in the office or out-patient department without the necessity of hospitalizing the patient. They may be inserted in locations where it is difficult to hold the element needles in place. The disadvantage of radium seeds lies in the fact that their even distribution throughout a large neoplasm may be difficult. They form point sources of radiation and there is a likelihood that under-irradiated areas may occur between the seeds which are sites for future recurrences.

Radium element needles are superior to radon seeds. The most useful needles are those in which the radium element is distributed over a distance of about 2 cm. A platinum-iridium alloy needle of 0.5 mm. wall thickness is very durable and this amount of filtration serves to exclude all beta radiation. Needles can be placed in more exact relationship, one to the other, than seeds and hence there is a more even distribution of radiant energy throughout the tumor. It is our practice to space needles about 1 cm. apart, giving a dose of approximately 200 mg-hr. per needle. In small neoplasms requiring only a few needles, this dosage may be considerably increased. It is rarely advisable to exceed a total of 2,000 mg-hr. In some locations, particularly the tonsil, it may be difficult to keep the needles in place; it is then necessary to resort to radon seeds.

Lesions on the floor of the mouth, the hard palate and the mucosa of the cheeks may often be satisfactorily treated by the intraoral application of radium imbedded in wax or dentists' modeling compound. The radium should be filtered sufficiently to remove all beta rays and a distance of about 1 cm. from the neoplasm should be maintained if possible. Normal structures are protected by lead plates and by so constructing the wax mold that they are at a greater distance from the source of radiation than is the neoplasm. Single doses of from 1,000 to 2,000 mg-hr. are employed, depending upon the size of the lesion. Larger doses may be given if the irradiation is extended over a period of several days.

With the advent of the high voltage shock-proof roentgen tube, apparatus of

great flexibility has become available. Not only may we treat with high voltages at short distances, but the roentgen beam may be easily and accurately directed at any angle. This has made possible the direct intraoral roentgen irradiation of neoplasms of the mouth, particularly those in the anterior portion. We have devised special lead cones for this procedure which are shown in Figure 1. The lower cone is made in several diameters to fit different size lesions. This cone is open at both ends and is inserted into the mouth like a speculum so that the tumor mass comes within its periphery. The upper cone is attached to the shock-proof head which is lowered until both cones are in apposition. The total distance from the focal spot of the tube to the tumor is 25 cm. This distance may, of course, be increased or decreased at will by making the upper cone longer or shorter. The other factors employed are

Fig. 1*a*. Lead cones for direct intraoral high voltage roentgen treatment. The lower cone is inserted into the mouth like a speculum. It is provided with a flange so that there will be no leakage of rays when the two cones are in apposition.

Fig. 1*b*. Cones in place ready to start treatment.

200 kv. with a filter equivalent to 0.5 mm. of copper. Single intensive doses of 1,500 to 2,000 r may be given to small lesions, or considerably larger doses may be administered to the more extensive tumors by the divided daily dose method. We have been using this technique for the past year and have obtained some very gratifying immediate results in carcinoma of the mucosa of the cheek and the anterior floor of the mouth. By combining this intraoral treatment with external cross-fire irradiation, the tumor obtains a more uniform dosage than is possible with radium and it is not subjected to the trauma of radium needle or seed insertion.

Following interstitial or direct intraoral roentgen irradiation of the primary lesion, external treatment should be instituted in most cases. In low grade malignancies of the anterior portion of the mouth, external irradiation may not always be necessary. No definite rules can be laid down regarding this matter, which must be left to the judgment and experience of the radiologist.

When the local lesion cannot be uniformly irradiated with a dose of 2,000 mg(mc)-hr. by needles or seeds spaced approximately 1 cm. apart, external irradiation should precede interstitial irradiation. Our experience with radium for external application has been very limited. We have relied almost entirely upon roentgen rays produced at 200 kv. (peak). Distances of 40 to 50 cm. have been employed. It has

FIG. 2. Epidermicidal reaction which follows a total of 2,400 r given in six consecutive daily doses of 400 r each.

not seemed advisable to use more than 0.75 mm. of copper filter. Heavier filters result in a slightly higher skin tolerance and a slightly greater depth dose, but cause a considerable reduction in the efficiency of the apparatus. All ionization measurements are made in air without back-scattering. A small portable electroscopic apparatus is employed which is periodically checked against our own open-air standard chamber. Needless to say, ionization measurements should be frequently and carefully made. It is our experience that the r output per minute is of little significance. We have operated machines at from 5 to 25 ma. and can see no difference in the results. If a short exposure at high amperage is given, it is of course essential that all factors be kept as constant as possible and that the timing be very accurate. There is much less chance of error with lower amperage and longer time.

The divided daily dose method is not new. It has been employed for years by many radiologists. It remained for Coutard to show us that we could obtain better results by employing total doses much larger than we had supposed it was safe to give. A large proportion of cases of carcinoma of the mouth occurs in the poorer classes and in most clinics it is not possible to hospitalize these unfortunates for a long period of time. We have therefore found it essential to institute a regimen which would fit the economic state of most of our patients. It has been our observation that daily doses of 400 r (measured in air) are fully as effective in treating oral malignancies as doses of 200 to 300 r which are more commonly employed. By using the larger daily dose, the total treatment period is considerably shortened. If 400 r is given through a portal of 100 sq. cm. for six consecutive days so that a total of 2,400 r is reached, an epidermicidal reaction will develop (Fig. 2). This reaction appears about a week or ten days following the completion of the series and is characterized by heavy crusting of the skin with patchy areas of moisture. The mucous membrane reaction begins a few days before the skin reaction and is characterized first by intense redness followed by the formation of a white membrane which goes on to exfoliation. During the height of the reaction, the patient may be extremely uncomfortable and may require opiates. The reaction produced by this dosage will, however, clear up in all instances. If one is to obtain lasting results, it is essential that a reaction of this severity be produced. If daily doses of 300 r are preferred, it will take approximately a total of 3,000 r to produce the desired reaction; that is, a treatment period of about ten days. If daily doses of 200 r are given, a total of about 4,000 r is necessary; that is, a treatment period of three weeks.

It is important that the patient be observed in three to four weeks following the completion of the series. At this time the reaction is subsiding, and if the tumor is radiosensitive, it should show definite regression. If no regression has taken place, it is our opinion that further irradiation is useless and will only add to the discomfort of the patient. However, if the response of

the neoplasm has been satisfactory and the patient's general condition warrants, further external irradiation should be given. It has been our practice to give one to three additional treatments of 400 to 600 r each; that is, a total of 400 to 1,200 r, depending upon the patient's local and general condition. Three to four weeks later this dosage of 400 to 1,200 r is again repeated. It is not wise to exceed a total much greater than 4,500 r by this method. If remnants of the local lesion persist after external irradiation, they should be treated by implantation of radium needles. In most cases, only one side of the neck is irradiated and in no instance is a field larger than 100 sq. cm. employed. If bilateral metastases exist, or if the disease-bearing area cannot be included within the 100 sq. cm. portal, the case is hopeless from the standpoint of cure. Palliative results may be obtained in such instances by employing small daily doses, but care should be taken not to produce a severe and uncomfortable reaction.

FIG. 3*a*. Carcinoma of the bucal mucosa with ulceration through the cheek and sinus formation.

FIG. 3*b*. Healing after high voltage external irradiation alone.

FIG. 4*a*. Epidermoid carcinoma Grade II mucosa of cheek with ulceration and sinus formation. Large metastatic cervical nodes.

Regression of movable, discrete cervical lymph nodes has frequently been observed, but when the disease has broken through the capsule of the nodes and they have become fixed, permanent control of the disease cannot be expected. Involvement of the bone offers an extremely bad prognosis, but in one case with extensive destruction of the mandible and pathological fracture there was regeneration of new bone and complete regression of disease following external irradiation alone. This patient has been well for three years.

In cases with ulceration through the skin and sinus formation, the outlook is also grave. However, such lesions may occasionally show a very satisfactory response (Figs. 3 and 4). Areas of leukoplakia are

FIG. 4*b*. One month later. The reaction following 2,400 r high voltage roentgen radiation is subsiding.

FIG. 4*c*. Patient clinically free of disease two years later.

radioresistant and are best treated by electrosurgical methods.

There are certain untoward sequelae of heavy irradiation which must be considered. A swelling of the parotid gland often develops after the first treatment and occasions the patient some annoyance. Much more troublesome is the extreme dryness of the mouth and loss of taste which often appears. These symptoms usually clear up in the course of time although it may take several months or even a year or two. A pouch-like thickening due

FIG. 5. Edema of the soft tissues of the anterior part of the neck following high voltage roentgen therapy.

to edema of the soft tissues in the submental region may follow heavy irradiation but disappears in the course of time. We have described this as a "turkey neck" (Fig. 5). Occasionally intractable pain from sclerosed cervical metastases may develop. We have not observed necrosis of the jaw from external irradiation alone, but it has occurred in some cases where radium was implanted in proximity to the jaw. This also applies to necrosis of cartilage.

Surgical procedures, even of a minor character, are dangerous following heavy

irradiation. A dissection of the glands of the neck is absolutely contraindicated. The tissues have no resistance to infection and before this was appreciated we observed several fatal results following attempts at block dissection of the glands of the neck. Even the extraction of teeth is dangerous. This is well illustrated by the case of a man who received heavy external irradiation for an epidermoid carcinoma involving the floor of the mouth. Two years later he was clinically free of disease, but had some pain referred to the lower incisor and bicuspid areas. The teeth in this region were extracted, following which the patient developed an extensive infection of the mandible and adjacent soft tissues which could in no way be controlled, and death shortly ensued. Repetition of the dosage which has been outlined is exceedingly dangerous and should not be attempted even after a lapse of several years.

It is, of course, important for the radiologist to follow his patients closely, and to become familiar with the reactions which result from various dosages. Having once established certain treatment factors such as voltage, filtration, distance, etc., it is essential that these factors be adhered to. A well known radiologist was recently asked why he employed such a heavy filter in the roentgen treatment of carcinoma of the mouth. His reply was that he had learned what that filter would do and it would take him at least three years to find out what a different filter would do.

Statistical results are dependent upon the selection of cases. If the radiologist limits his treatments to the so-called "operable" group, his results will compare favorably with those obtained by surgery. However, the radiotherapist soon learns that he can make no selection of cases. Many of the patients who at the outset appear the most unfavorable will do the best. If all cases of carcinoma of the buccal cavity are irradiated, one may expect to obtain permanent regression of the disease in 10 per cent, and very gratifying palliative results in a much larger number.

TREATMENT OF OTITIS MEDIA AND MASTOIDITIS BY THE ROENTGEN RAY

ANALYSIS OF FIFTY CONSECUTIVE CASES

By JOSEPH H. LUCINIAN, B.S., M.D.
Roentgenologist, Victoria Hospital; Visiting Roentgenologist, Jackson Memorial Hospital
MIAMI, FLORIDA

ACUTE or chronic otitis media with or without mastoid complication presents a serious problem for all concerned. Discharge, pain and impaired hearing, often of years' duration, are not uncommon after spontaneous perforation or even following operation. Any method of treatment which will avoid perforation, render operation unnecessary or lessen discharge and pain is very desirable.

Careful search of the literature revealed that roentgen rays were used in the treatment of otitis media by Dionisio[7] thirty years ago. Radiation treatment proved successful in 75 per cent of his 20 cases. Beattie[1] reported complete cure in 14 cases of subacute and chronic otitis media in adults and improvement in 4 cases in infants. Dempster[3] obtained favorable results in 15 cases. In 1922, Szasz[17] and in 1923, Raynal[14] reported improvement in a smaller series of 11 cases of chronic middle ear and mastoid infection associated with deafness. Complete cure was obtained in 33 out of 35 cases by Grande[10] in 1925. In 1926, Di Donato[6] reported progressive diminution of discharge and complete disappearance of bacteria in the discharge of 75 cases of chronic suppurative otorrhea. Granger[11] treated 30 cases of mastoiditis in infants in 1931 with gratifying results. He cautioned against roentgen treatment of mastoiditis with bone destruction. Schillinger[16] did not consider bone destruction a contraindication to roentgen treatment. He claims to be the first who deliberately treated mastoiditis with the roentgen ray in the presence of bone destruction as shown by clinical and roentgenological evidence. In a series of 38 cases he obtained 85 per cent cures. The remaining 15 per cent failed to respond and were operated upon. However, he is of the firm belief that in a very great majority of cases of mastoiditis, operation can be avoided provided radiation treatment is given early. Goldmann,[9] in reporting a selected series of cases, makes the prophetic remark that radiation therapy will materially limit the field of surgery in mastoiditis. Cherniak and Gorodetzky[2] observed that 5 cases which had been given preoperative irradiation showed definite limitation of the inflammatory process. These authors advocate radiation therapy for the improvement of the general condition and the relief of pain prior to operation.

PATHOLOGY AND CLINICAL MANIFESTATIONS

Inflammation of the middle ear and mastoid, like inflammation elsewhere, is characterized by congestion, lymphocytic and leukocytic infiltration, suppuration and finally resolution in the uncomplicated cases. Chills are not uncommon, fever is extremely variable; it may be entirely absent or it may rise as high as 105° F. Wolf[19] has recently called attention to a type of mastoiditis which he designates "silent mastoiditis." The symptoms and signs are almost entirely masked and the mastoid process may undergo complete destruction before the true nature of the condition is recognized. Pain is always present in a variable degree and is usually throbbing and continuous. Tenderness may almost always be elicited at the site of the emissary veins and the tip of the mastoid. Occasionally there is postauricular swelling. Headache, nausea and vomiting are inconstant. Discharge, at first odorless, mucopurulent,

scanty and watery, becomes profuse, thick, purulent and offensive. Leukocytosis is present and may be greatly elevated in the presence of mastoid complication.

THE RATIONALE

The uniformly favorable results obtained by roentgen treatment in inflammatory processes elsewhere form the logical basis for the treatment of acute, subacute or chronic otitis media and mastoiditis by the roentgen ray. Experience in this field of therapy extending over a period of thirty years has shown conclusively that roentgen radiation applied early will promptly relieve pain, reduce fever and gradually bring about the disappearance of discharge. Perhaps empirical at first, there is a well-founded scientific basis for the uniformly successful results obtained by roentgen treatment. It is well known that of all the body cells, lymphocytes are the most sensitive to roentgen rays. Heineke,[12] and later Warthin,[18] showed experimentally that as early as fifteen minutes after roentgen treatment lymphocytes undergo nuclear disintegration which continues for several days. Desjardins[4] has shown that with the disintegration of lymphocytes, pressure is relieved and with the relief of pressure, pain is relieved. Lymphocytic infiltration being a major and constant feature in inflammation of the middle ear and mastoid, it becomes quite apparent how roentgen rays relieve pain, sometimes within twenty minutes after a single exposure. Warthin has demonstrated another important action of roentgen radiation in inflammatory processes, namely, the promotion of phagocytosis. He has shown microscopically that phagocytosis of broken nuclear chromatin particles is most active following irradiation and continues for several days until the lymphocytes are almost entirely destroyed. He has further shown that these ingested particles in phagocytes are most numerous at first and gradually diminish in number. The polymorphonuclears and eosinophiles undergo disintegration somewhat less rapidly but continue for two or three days.

In addition to the destruction of lymphocytes and promotion of phagocytosis roentgen rays are said to liberate enzymes, antibodies and other unknown principles which promote autolysis and liquefaction. Concerning the bactericidal action of the rays, Di Donato[6] has demonstrated that, following roentgen treatment, cultures from the pus of the middle ear and mastoid show gradual diminution and finally complete disappearance of bacteria. Clinically, it has been observed that more rapid response to irradiation takes place in the more acute cases, presumably in the period of richest lymphocytic infiltration. We have observed further that roentgen radiation applied to the ear and mastoid destroys lymphocytic hyperplasia in and about the orifice of the eustachian tube, thus relieving obstruction, restoring the function of hearing to normal and removing a very probable source of reinfection. The action of the roentgen ray in chronic otitis media is analogous to its action in tuberculous adenitis and actinomycosis. In these chronic inflammatory processes, this treatment causes hyperemia, improves the circulation, breaks down and produces the absorption of chronic fibrous tissue.

DOSAGE AND TECHNIQUE

With few exceptions the authors referred to advocate a small dosage at moderately low voltages and with light filtration. This is rational in view of the superficial localization and the highly radiosensitive nature of the inflammatory exudate. Goldmann[9] prefers a higher voltage and a heavier filtration of 0.3 to 0.5 mm. of zinc plus 1 mm. of aluminum. The technique used in my work has undergone considerable change during the past several years with corresponding improvement in the results.

At the present, I employ the following technique: 100 to 110 kv.; 16 inch distance; 2 mm. aluminum; 5 ma.; five minutes; a tube with a broad disk for target with an output of 14.3 roentgens per minute; the total dose is 71.5 r, measurements taken in air. This is the equivalent of about 15

TABLE I

CASES OF OTITIS MEDIA AND MASTOIDITIS TREATED BY ROENTGEN RAYS

Case No.	Name	Sex	Age	Ear	Mastoiditis	Duration Before Roentgen Treatment	Pain	Temperature	Discharge	No. Treatments	Mastoidectomy	Improved or Cured	Remarks
I	D.W.	F	23	L		2 yr.			+	3		I	Discontinued treatments.
II	B.W.	F	36	B		10 yr.			+	3		I	Less discharge; hearing improved.
III	I.B.	M	36	L		4 da.	++		+	1		C	
IV	V.W.	F	5	R		10 da.	++	104°	+	2		C	
V	P.Y.	F	14 m	B		10 da.	+		+	1		C	
VI	M.V.	M	13 m	R		1 wk.	+	+	+	1		C	
VII	E.R.	M	4 m	B		2 wk.	+	+	+	3		C	
VIII	C.R.	M	19 m	B		3 wk.	+	+	+	4		C	
IX	J.R.	F	42	B		4 wk.	+	+	+	4		I	Tinnitus relieved.
X	F.O.	F	12 m	B		3 mo.	+	+	++	4		C	Diabetes of 14 yr. duration.
XI	C.R.	F	58	R		1 mo.	+			1		C	No recurrence of boils in canal.
XII	D.M.	F	3	L		10 da.	+	+	++	2		C	Operation obviated.
XIII	J.L.	M	5	B		5 da.	+	+	+	3		C	
XIV	G.M.	F	7	B		2 wk.	+	+	+	2		C	
XV	A.S.	F	20 m	B		18 mo.	+	105°	++	6		C	Distressing eczema cured.
XVI	W.J.	M	8	R		3 wk.	+		+	2		C	
XVII	J.I.	M	2	B		5 da.	+	+	+	2		C	
XVIII	R.G.	M	3	B	B	2 wk.	+	+	+	4		C	Operation obviated.
XIX	A.G.	F	8	B	B	6 yr.	+	+	+	6		C	No recurrence of discharge.
XX	S.F.	M	6½	L		1 wk.	+	102°	+	2		C	
XXI	D.C.	F	3	B		1 wk.	+	+	+	6		C	
XXII	A.B.	F	6 m	B		2 wk.	+	+	++	2		C	
XXIII	A.J.B.	F	22 m	B		2 da.	+	+	++	3		C	
XXIV	J.A.	F	3 m	B		10 da.	+	+	+	4		C	
XXV	F.S.	M	54	L		1 wk.	+		+	2		C	
XXVI	G.McK.	F	15 m	B		7 da.	+		+	2		C	
XXVII	J.C.R.	F	24	B	B	4 mo.	++	+	+	6	+		Pregnancy; operation; recovery.
XXVIII	L.R.	M	36	L	L	12 yr.			+	1			Discontinued treatments.
XXIX	F.L.	F	13	L	L	2 yr.	+	+	+	5		I	Discharge and deafness relieved.
XXX	P.Y.	F	14 m	B		2 wk.			+	2		C	
XXXI	A.W.	M	6	R		2 wk.	+	+	+	2		C	
XXXII	L.R.	M	12 m	B		3 wk.	+	+	+	2		C	
XXXIII	B.S.	F	7½	L	L	6 yr.	+	+	+	5		C	Perforation, deafness completely relieved.
XXXIV	J.L.	F	4	L		5 da.			+	1		C	
XXXV	N.F.	M	3 m	B		7 da.	+	+	+	1		C	
XXXVI	C.O.	M	6 m	B		2 yr.	+	+	+	2		C	
XXXVII	R.F.	M	40	L		9 da.	+		+	1		C	
XXXVIII	N.S.	F	5	L		2 wk.	+	+	+	1		C	
XXXIX	M.B.	M	7	L		1 wk.	+		+	2		C	
XL	W.H.A.	F	50	L	L	2 yr.	+	+	+	3		C	Chronic discharge stopped.
XLI	I.C.	M	48	R	R	1 yr.	+	+	+	1	+		Escaped observation following operation.
							+	+					
XLII	J.P.	F	22	B		1 wk.	+	+		3		C	Perforation obviated; tinnitus relieved.
							+	+					
XLIII	J.D.	M	55	R		3 da.	+	+		1		C	Perforation obviated.
XLIV	J.L.	M	8	R		1 wk.	+	+	+	1		C	No recurrence (see text).
XLV	C.L.	M	37	L		3 da.	++	+		5		C	No perforation.
XLVI	D.H.	M	5 m	L	L	10 da.	+	103°	+	2		C	Operation obviated.
XLVII	R.K.	M	27	B		1 mo.	+	+	+	4		C	
XLVIII	R.F.	M	19 m	B		3 da.	+			2		C	Perforation obviated.
XLIX	M.J.	F	7	B		20 da.	+	+	+	2		C	
L	T.S.	M	15 m	R		2 da.	+	+	+	2		C	

M = Male; F = Female; L = Left; R = Right; B = Both; I = Improved; C = Cured.

to 20 per cent of the erythema dose. In my experience, no harm has resulted to the organs of hearing with this quantity of rays.

NUMBER OF TREATMENTS

My experience agrees with that of most of the authors in that a single treatment is all that is required to bring about complete

cure in the great majority of the acute cases. This result is based on the observation that radiotherapy is most effective during the infiltrative and less during the suppurative stage. Several cases in the subacute stage have required two but never more than three treatments; whereas, chronic cases of several months' or years' duration have been given three to six treatments to effect a cure. Ross,[15] on the other hand, believes that roentgen radiation should be applied repeatedly every eight to twelve hours until relief is obtained. The treatments are administered at three day intervals at first, and with the progressive improvement the periods are extended from seven to ten days apart. In the very chronic cases it is my practice to give the treatment at weekly intervals. A cone of sufficient diameter is used to cover a portion of the normal area about the ear and mastoid.

In a series of 50 cases I have encountered no complications such as parotitis, epilation or injury to nerves, which complications are not infrequent following operations on the mastoid. Aside from the safety of the roentgen treatment as compared with operation, there has been complete absence of recurrence of the infection for as long as three years in this series of cases.

ANALYSIS OF CASES

This presentation is based on a series of 50 consecutive cases of otitis media and mastoiditis, treated in my office during the past several years, the salient features of which may be found in Table 1. The sexes were about equally divided. The youngest patient was three months and the oldest was fifty-eight years of age. The right ear was involved in 9 cases, the left in 15 cases and both ears in 26 cases. Nine cases were complicated by mastoiditis; 6 of them were examined roentgenologically and evidence of the disease was demonstrated, 2 of which were operated upon. In the majority of cases, the duration was from several days to two weeks. In a small number it was from several weeks to several months, and in still fewer from two to twelve years. There were 31 acute, 8 subacute and 11 chronic cases. The temperature range was from 99.6 to 105° F.

Of the acute cases, 12 required only one treatment, and 18 cases two treatments for complete relief. The chronic cases received as many as six treatments each. Early roentgen treatment obviated apparently impending perforation in 4 cases, and in 3 mastoidectomy became unnecessary after operation had been seriously considered.

RESULTS

Pain. In a series of 50 consecutive cases pain was consistently relieved following the first application of the roentgen ray. With the relief of pain the patient was able to sleep perhaps for the first time in several days. There was complete change in the facial expression, the patient became less irritable, more cheerful and submissive to the usual manipulation of the ear.

Fever. The drop in the temperature was more gradual than the relief of pain but usually disappeared within ten to fifteen days. Persistently high temperature or secondary rise indicates reactivation of the infection. It may be due to extension of the infection to the mastoid process. This has been encountered only once in my series. There may be a minor secondary rise which usually subsides following the second or third roentgen exposure.

Discharge. Several authors report a gradual but steady decrease in the amount of the discharge. My experience is in agreement with that of Ross[15] and Granger[11] in observing an initial increase after the roentgen treatment followed by gradual diminution. Roentgen therapy seems to facilitate the flow of secretion from the ear more than any other method of treatment. With establishment of free drainage there is less danger of incidental mastoid infection. The discharge underwent changes in consistency, odor and quantity; became thinner, less offensive and more profuse.

Tympanic Membrane. Through the cour-

tesy of Dr. M. D. Kirsch I am able to communicate his observations of the changes of the tympanic membrane from hour to hour and from day to day. Following the first roentgen treatment the swelling and redness of the drum membrane and canal rapidly decrease; there is more room in the canal and more of the membrane can be seen. Early radiotherapy shortens the course of the inflammation and obviates drum perforation. Where perforation already exists it does not present its former angry appearance. There is a decided decrease in the pulsations of the perforation. In about two to three weeks with the complete cessation of discharge the drum membrane heals entirely, has a pearly appearance and the light reflex shows itself as before.

Tenderness. Soreness and tenderness are markedly reduced within forty-eight hours following roentgen treatment.

Hearing. Hearing, always impaired to varying degrees, is improved within twenty-four to forty-eight hours and is completely restored to normal with healing of the drum membrane. Tinnitus, annoying subjective noises, headache and dizziness are also relieved.

Mastoid Complications. Schillinger,[16] Goldmann,[9] and Cherniak and Gorodetzky[2] have emphasized the importance of early radiotherapy of otitis media for prevention of mastoiditis. Granger[11] has treated 30 cases of mastoiditis, all of which recovered without resorting to operation. Dr. Carl Dunaway, in a personal communication, has stated that with the timely application of the roentgen ray the need for surgery has been markedly reduced and that within the last year he has not found it necessary to operate on a single mastoid case.

In our own series no case developed acute mastoiditis after commencement of roentgen treatment. There were 9 instances of mastoiditis before the roentgen treatment was begun. Two of the 9 cases were operated upon and 7 recovered without operation.

CHRONIC OTITIS MEDIA AND MASTOIDITIS

The response of chronic otitis media and mastoiditis to roentgen therapy is somewhat slower than in the acute cases but improvement is positive, progressive and follows the same sequence. Pain and tenderness, usually deep and dull, are the first to disappear. The temperature, usually slight but continuous, returns to normal within three to five weeks. The discharge, sometimes of months' or years' duration and usually thick, purulent and extremely offensive, is the next to disappear. The drum membrane, sometimes as much as 50 per cent destroyed, shows gradual and complete healing within four to five weeks. The hearing, often markedly impaired, is also restored to normal.

CONTRAINDICATIONS

There are no clear cut contraindications to treatment of otitis media and mastoiditis by the roentgen ray. In certain stages the prophylactic use of the rays may be limited. Even in the presence of high temperature, high leukocytosis, thick, ropy discharge, sagging of posterior wall and narrowing of posterior canal indicative of mastoid involvement, no harm can and some good may result from radiotherapy. However, one is not justified in entertaining a false sense of security in the presence of surgical mastoiditis, particularly in acute and fulminating cases.

CONTROL SERIES

In Table II is presented a series of 25 unselected cases through the courtesy and from the records of Dr. M. D. Kirsch. These cases received no roentgen treatment, with the exception of Case VI, which received radiotherapy after one year. Case IV, a man twenty-two years of age, who had been suffering from intense and agonizing pain for three weeks, was relieved promptly following a diagnostic roentgen examination. The duration of illness varied from one week to fifteen years. Eleven patients were subjected to tympanotomy. In

7 cases there was mastoid involvement and in 2 cases mastoiditis developed as a late complication. Five cases including 2 of the 11 had mastoidectomy with complete recovery. Five cases had spontaneous perforation. In 2 cases otitis media followed sinusitis and in 2 others tonsillitis was the exciting cause; after appropriate treatment these patients recovered. Five cases have shown no tendency to heal; either the tympanum has not healed, discharge persists or hearing is impaired.

Table II

CONTROL CASES NOT TREATED BY ROENTGEN RAYS

Case No.	Name	Sex	Age	Ear	Mastoid	Duration	Operation	Complication	Form of Treatment	Remarks
I	F.J.	M	4	L		7 wk.	T		I & M	High fever 3 wk. Profuse discharge.
II	F.M.	M	8	L		5 wk.	T		I & M	Profuse discharge; recovery.
III	H.E.N.	F	11	R		6 wk.		Perforation	I & M	Followed tonsillitis. Repeated tympanotomy for drainage.
IV	O.F.	M	22	R		7 wk.	T		I & M	Intense pain 3 wk., relieved in 24 hr. after diagnostic x-ray.
V	H.F.	F	6 wk.	B		5 wk.	T		I & M	Uneventful recovery.
VI	A.L.	F	13	L	+	1 yr.	T	Mastoiditis	I & dry powder	Profuse drainage—chronic mastoid. 1 yr. later x-ray treatment; ear dry, mastoid clear.
VII	J.J.T.	F	66	R		5 yr.		Perforation	Dry powder	Constant discharge—no recovery.
VIII	J.S.	F	5	R	+	1 wk.	Mastoidectomy	Mastoiditis		Acute and fulminating; week later mastoidectomy—see below.
IX	J.S.	F	5	L	+	1 mo.	Mastoidectomy	Mastoiditis		Left mastoiditis while recovering from right mastoidectomy. Left mastoidectomy.
X	J.L.	M	28	L		4 mo.	T	Mastoiditis		Mastoidectomy; recovery.
XI	M.B.	F	49	R	+	3 mo.		Mastoiditis		Profuse discharge; drum never healed; ear dry eventually.
XII	H.H.T.	M	2½ mo.	R		3 wk.			I & M	No complications; recovery.
XIII	C.Mc.	M	72	L		3 mo.	T		I & M	Recovery; drum normal.
XIV	C.C.D.	F	31	R	+	4 yr.		Mastoiditis	Dry powder	Hearing nil. Large polyp removed. Foul discharge persists.
XV	B.E.	M	18	B	+	15 yr.	Mastoidectomy	Mastoiditis	Dry powder	No improvement. Intracranial complications. Radical left mastoidectomy.
XVI	A.I.	M	21	R		6 wk.		Perforation	Irrigation	Healing in 6 wk.
XVII	K.L.	F	19	R		4 wk.		Perforation	Irrigation	Healing in 4 wk.
XVIII	O.L.	M	2	L		5 wk.	T	Mastoiditis	Irrigation	Ear dry; drum not healed—acute mastoiditis; operation, recovery.
XIX	Z.S.	F	3	B		2 mo.		Perforation	Irrigation	Recovery both ears.
XX	S.N.	F	40	B		6 wk.	T	Sinusitis	Irrigation	Otitis media followed acute sinusitis; recovery.
XXI	A.B.S.	M	25	L		8 mo.		Chronic tonsillitis	Dry powder	Chronic discharge. Recovery after tonsillectomy.
XXII	S.S.	M	4	R		4 mo.		Tonsillitis	Irrigation	Recovery after T. & A.
XXIII	D.K.	F	30	L		1 yr.		Sinusitis	Dry powder	Recovery after radical antrum.
XXIV	C.S.	F	7	L		5 mo.	T		Dry powder	Complete destruction of drum following scarlet fever.
XXV	P.G.	M	7	R	+	1 yr.	T	Mastoiditis	Irrigation later dry powder	Perforation dry; mastoidectomy not necessary.

M = Male; F = Female; L = Left; R = Right; B = Both; T = Tympanotomy; I & M = Irrigation and medication.

CASE HISTORIES

Case IV. V. W., a girl, aged five, was seen July 28, 1934. Ten days previously the patient was awakened from her sleep complaining of intense earache which continued for several days. The temperature, which was 104° F., dropped to 101° F. on incising the right ear drum and fell to 99.4° F. the next morning. However, by afternoon of the same day it again rose to 103° F. There was no chill or vomiting. Under gas anesthesia the drum was incised again with marked relief of pain. The temperature continued at 103.6° F. and the discharge was very profuse. Following the first roentgen treatment the temperature dropped to 101.4° F. and the patient was more cheerful and wanted to play. On July 30, the temperature was 102° F., discharge thick, yellow and less profuse. The patient's condition was decidedly better. On August 1, the second and last roentgen treatment was given, followed by con-

tinued improvement in the patient's appearance. The temperature remained normal and discharge became scanty. On August 10, the patient was discharged completely cured.

Case xv. A. S., a girl, aged twenty months, had had discharging ears since she was six weeks old. The drum membranes were incised on eight different occasions. In the latter half of 1933 the patient was free from earache and discharge for six months. On December 5, 1933, the patient contracted a severe cold. On December 7 both ears began discharging spontaneously. The temperature continued at 103° F. for a week, at which time it rose to 105° F. On December 26, 1933, the first roentgen treatment was applied. On December 27, 1933, there was some improvement in the patient's general condition but the discharge was pouring out continuously. The irritating discharge from the ear had excoriated the skin within and without the ear canal. Following the second roentgen application the eczematous condition was completely healed. The temperature was normal; the patient looked brighter and felt better. January 13, 1934, the third and last roentgen treatment was given and on January 20 there was complete absence of discharge and pain.

Case xxvii. Mrs. J. R., aged twenty-four, four months' pregnant, had had bilateral discharging ears for the past fifteen weeks. When seen the patient's chief complaint was constant and throbbing pain and partial deafness in both ears. Her temperature was 102° F. and there were marked tenderness and edema over the mastoid processes. Roentgenogram of both mastoids showed bilateral infection with moderate bone destruction. Because of her pregnant condition the patient preferred a more conservative type of treatment than an operation which she was urged to undergo. Following the first roentgen treatment the patient experienced marked relief from pain and slight improvement of hearing. There was profuse, mucopurulent discharge from both ears. The roentgen treatment was repeated at five day intervals but the tenderness, edema and discharge persisted. The patient submitted to bilateral simple mastoid operation and made an uneventful, complete recovery.

Case xxxiii. B. S., a girl, aged seven and a half, gave a history of pain and discharge from the left ear of six years' duration. At eighteen months of age she underwent a mastoid operation, since which time she has had thick, yellow, offensive and purulent discharge. She complained of dull constant pain in her left ear with gradually increasing deafness. The patient was poorly nourished, underdeveloped, nervous and extremely irritable; her temperature was 99.6° F. but at times it had risen to 101° F. She was taken to various clinics in different cities and received treatment over a period of six years but without material improvement in the hearing or permanent decrease in the discharge. One week after the first roentgen treatment the patient experienced slight relief from pain but the discharge became thinner and more profuse. She continued to run a low-grade fever. There was no decided change in the tympanic membrane which was destroyed more than 50 per cent. Treatments were applied at weekly intervals and at the end of six weeks the fever, pain and discharge completely disappeared. The hearing returned to normal and the membrane healed and became pink and pearly in appearance. The patient was seen six months later and examined by Dr. M. D. Kirsch who found the left ear perfectly dry and healed and the hearing normal on both sides. The patient had gained considerable weight, seemed more cheerful and very slightly nervous.

Case xliv. J. L., a boy, aged eight, gave a history of frequent colds complicated by recurring otitis media during the past three to four years. He had had the attacks several times during the year, requiring incision and drainage lasting several weeks. The present illness began one week previously following a severe cold. Three days before the drum membrane had been incised and free drainage obtained but the perforation had closed. The patient complained of earache, headache and tenderness back of the ear. The temperature was 99.6° F. and the discharge was yellow, green mucopus. Following the first and only roentgen treatment pain, fever and discharge completely disappeared and within one week the drum membrane was entirely healed. The patient has been under observation for the past six months and during this period has had no colds or recurrent otitis media.

SUMMARY

Fifty cases of otitis media (31 acute, 8 subacute, 11 chronic) were given roentgen

therapy over the ear and mastoid area. The treatment was consistently followed by relief of pain, increased discharge, improved hearing and amelioration of the systemic manifestations of the disease. After the treatment none of the acute cases developed mastoiditis or perforation of the drum, and none of them required tympanotomy. Mastoiditis was already present when the rays were applied in nine cases, two of which later required mastoidectomy.

The symptoms associated with chronic otitis media such as persistent discharge of years' duration, pain, tinnitus and deafness were improved or eradicated. The healing of perforated tympanic membranes seemed to be definitely accelerated. Observation of these cases indicates that the earlier in the stage of the disease the treatment is applied, the more rapidly the improvement appears to take place.

In a series of twenty-five unselected cases of acute and chronic otitis media in which roentgen therapy was not applied, perforation of the drum occurred in five, mastoiditis developed in nine, mastoidectomy had to be done in five and tympanotomy in eleven.

It appears, therefore, that roentgen therapy, properly applied, in both acute and chronic otitis media, shortens the course of the disease and prevents complications. In no case was a deleterious effect observed.

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ADVANCED CANCER OF THE HEAD AND NECK*

By CHARLES L. MARTIN, E.E., M.D., F.A.C.R.
Professor of Radiology, Baylor Medical School
DALLAS, TEXAS

TUMOR clinics are constantly confronted with the care of large, unsightly, evil smelling carcinomas of the head and neck. They may involve only the skin or extend into the sinuses, nose, orbits, mouth or cranial vault as well as the subcutaneous tissues. Primary lesions in the larynx and nasopharynx often produce large masses in the neck but they have been dealt with in a previous article[4] and will not be considered here. All of these neoplasms, with few exceptions, arise from squamous epithelium and they eventually extend to the glands of the neck.

The efficiency of low voltage roentgen rays and heavily filtered radium used in adequate doses in the care of squamous cell carcinoma of moderate size has been emphasized in a previous paper.[3] However, such methods are not always applicable to the large neoplasms about the head and this is especially true when bone and cartilage are involved. Widmann[10] has obtained some striking regressions by applying from 2,500 to 10,000 r to large lesions about the face using unfiltered roentgen rays and an intermediate voltage, but he advocates the additional use of heavily filtered radium packs when the lesions are indurated or deep seated.

In our own clinic an effort has been made to perfect techniques which can be carried out in hospitals of moderate size where standard equipment is available. When Coutard first described his method, its advantage, namely, the destruction of carcinoma cells with a minimum of damage to normal structures, made it seem ideal for use about the head where an effort must be made to save the delicate structures in the eye, nose and throat as well as the bone and cartilage. However, the French plan was found to be too time-consuming for a busy clinic and acting upon the suggestions of Zwerg[11] and Borak[1] a much higher irradiation intensity was adopted, thereby shortening the time of each exposure. This was brought about by a reduction in filtration. Since Coutard's published carcinoma doses applied only to malignant tumors of the throat which are very radiosensitive, it seemed desirable in the beginning to establish a dose capable of eradicating a large carcinoma of the face. One of the first test cases was described in a previous article.[6]

The tumor measured 3 inches in diameter and was situated high up on the right cheek as illustrated in Figure 1. The underlying malar bone was definitely invaded over most of its outer surface. The pathological report was epidermoid carcinoma, Grade III. No palpable lymph nodes could be found. A total of 3,600 r (measured in air without back-scattering) was delivered to this lesion through a portal measuring 10 cm. on a side during a period of thirteen days. A treatment consisting of 300 r was given every day except Sunday. The factors were: 200 kv., 6 ma., a target skin distance of 50 cm., and a filter of 0.75 mm. of copper and 1.0 mm. of aluminum. The tumor had completely disappeared in two months but the defect in the bone remained and required about six months for complete healing. No surgery of any sort was done and this case remains entirely well at the end of two years and two months. Each daily treatment was given in twenty-five minutes (12 r per minute) and the entire series was finished in two weeks. No bone or skin damage can now be made out and enough cases have now been treated to convince us that 3,600 r is a very efficient dose under the above conditions.

In an effort to further increase the efficiency of the department a machine operating at 25 ma. was installed and it was found that 300 r could be delivered with this apparatus under the above conditions in seven and a half minutes (40 r per minute).

* Read at the Twenty-first Annual Meeting, American Radium Society, Kansas City, Mo., May 11–12, 1936.

Fig. 1. Epidermoid carcinoma, Grade III, involving bone treated with 3,600 r given in thirteen days with a filter of 0.75 mm. of copper and 1.0 mm. of aluminum and an intensity of 12 r per minute. The middle photograph was made in three months and the one on the right in two years and two months after the treatment was given. The right eye had been taken out many years previous to his present trouble.

A test case was then treated in an effort to determine the comparative value of the higher intensity.

In this instance the carcinoma which measured about 3 inches in diameter was situated on the lower cheek and it extended deep into the masseter muscle. There was also some involvement deep in the neck behind the angle of the jaw. The pathological report was epidermoid carcinoma, Grade II. A dose of 300 r was given each day except Sunday until a total of 3,600 r was delivered. The results are illustrated in Figure 2. Although the main lesion completely disappeared a small ulcer remained on the cheek during six months of observation. The residual lesion was finally resected and found to contain malignant cells. This partial failure was thought to be due to improper dosage at the bottom of a large tumor rather than to the increased intensity.

However, the good result obtained with the first test case induced us to reduce the

Fig. 2. Epidermoid carcinoma, Grade II, involving masseter muscle and glands of the neck treated with 3,600 r given in fourteen days with a filter of 0.75 mm. of copper and 1.0 mm. of aluminum using an intensity of 40 r per minute. At six months the small ulcer shown on the right was still present and when it was resected its wall contained carcinoma cells.

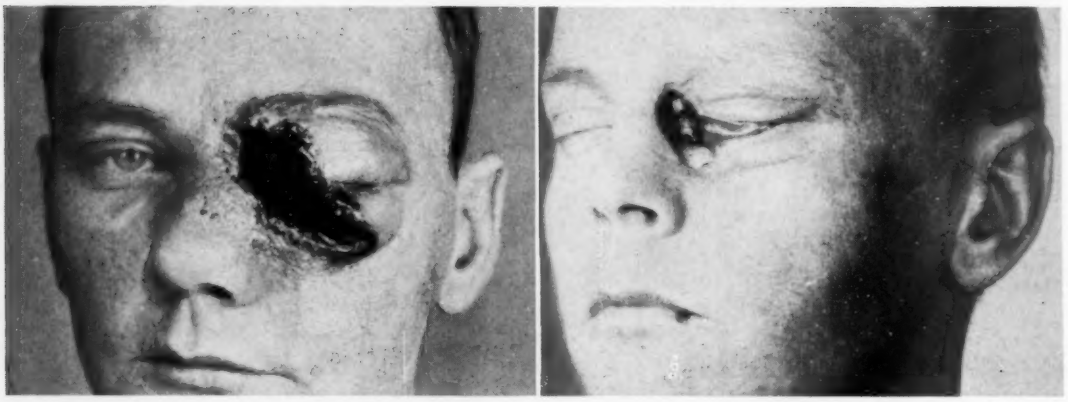

Fig. 3. Epidermoid carcinoma, Grade III, extending deep into the ethmoid sinuses, destroying the wall of the nose and causing blindness of the left eye although the eyeball was not damaged; 3,000 r was given over the lesion and the orbit in fifteen days using a filter of 0.8 mm. of tin, 0.25 mm. of copper and 1.0 mm. of aluminum with an intensity of 15.6 r per minute. The photograph on the right made two months later shows no evidence of the tumor. The eyeball was not damaged and the eyebrow was not completely epilated.

intensity somewhat. The work of Merritt and Rathbone[7] indicated that increased filtration should give a greater differential effect and make the use of heavy dosage safer when cartilage and bone are in the field, and for this reason the reduction in intensity was brought about through the use of heavier filters. At first 2 mm. of copper and 1 mm. of aluminum were used but when it was found that 300 r could be obtained with the heavy Thoraeus filter (0.8 mm. of tin, 0.25 mm. of copper and 1.0 mm. of aluminum) in nineteen and a half minutes using 220 kv. and 20 ma. at 50 cm. distance, it was adopted for all work about the head. The intensity with these factors is reduced to 15.6 r per minute. A limited experience with this technique leads

Fig. 4. Epidermoid carcinoma of the skin with extensive destruction of the cartilage of the ear treated with 3,300 r given in twelve days using a filter of 0.75 mm. of copper and 1.0 mm. of aluminum and an intensity of 40 r per minute. The middle photograph made two months later shows the exposed edge of a strip of painful partially necrotic cartilage. After its surgical removal the lesion healed promptly as shown in the photograph on the right.

us to believe that the increased filtration tends to protect normal tissues. Case III illustrates its value.

This young man had a carcinoma which extended deep down into the ethmoids from which it probably arose. Although the left eyeball looked normal it was sightless because of pressure on the optic nerve from tumor tissue in the back of the orbit. The lids were much swollen and tumor tissue could be felt beneath the skin overlying the left antrum. The cartilage of the nose was completely destroyed over an area about 1 inch in diameter. Tissue removed from deep in the ethmoid region was diagnosed as epidermoid carcinoma, Grade III. Much purulent drainage came from the ulcer and a tender gland felt beneath the left mandible was thought to be inflammatory. During a period of fifteen days, 3,000 r was delivered to a portal measuring 10 cm. on a side and including the left eye and the nose. During a period of twelve days 2,100 r was delivered over the left mandible using a 10 cm. portal. The dose of 3,000 r was used because our pathologist felt that the tumor was very radiosensitive and it seemed desirable to produce a minimum reaction. The skin about the lesion showed some reddening but no ulceration. At no time did the eye show a conjunctivitis, and at the end of two and a half months Dr. James T. Mills was asked to clean out the dead bone in the treated area so that a skin graft might be attempted. Histological examination revealed no carcinoma in any of the tissues removed. The cartilage of the nose was not damaged and neither was the skin.

Fig. 5. Extensive epidermoid carcinoma, Grade III, involving the side of the face and the glands of the neck. The treated area measured 20 cm. in length and received 4,200 r in thirty days with a filter of 0.75 mm. of copper and 1.0 mm. of aluminum and an intensity of 40 r per minute. The malignant tissue melted away but a tough grayish tissue remained at the end of three months as shown in the photograph on the right.

Some may contend that the same result could have been obtained with low filtration but such has not been our experience.

In Case IV, 3,300 r was administered during a period of twelve days using daily doses of 300 r delivered to an area measuring 12 by 8 cm. laid out to include the epidermoid carcinoma involving the ear. A filter of 0.75 mm. of

FIG. 6. Large epidermoid carcinoma, Grade 1, involving the entire right cheek, alveolar margin and corner of the mouth treated with a combination of long, weak, platinum radium needles implanted for seven days and 2,100 r applied externally to the cheek in seven days using a filter of 2.0 mm. of copper and 1.0 mm. of aluminum and an intensity of 20 r per minute. The illustrations show the epidermolysis, which was completely healed at the end of three months. There was a complete loss of pigment in the treated area.

copper and 1 mm. of aluminum was used with an intensity of 40 r per minute. The regression of the carcinoma was quite satisfactory but at the end of two months it was found necessary to dissect out the remaining fragments of partially necrotic cartilage to obtain complete healing.

Enough such cases have occurred in our practice to make us believe that the heavy filtration is desirable. Although intensity may not enter into the problem we have observed that our best results have been obtained with rates varying from 12 to 16 r per minute.

Carcinomas about the head often reach large dimensions and we have found that when low filtration is used the dosage must be graded in accordance with the size of the area irradiated. Case v illustrates the sequelae resulting from the use of large doses over large areas.

This patient came to Baylor Hospital after having received treatment for four months at the hands of a "cancer healer" who broadcasts regularly from a powerful radio station in Mexico. At the time of admission the ulcerated area on the temple measured 1½ by 2½ inches and was continuous with a second area measuring 3 inches in diameter on the cheek. Glands were felt in the neck and a hard mass attached to the clavicle measured 2 inches in diameter. Specimens removed from the edges of the ulcers were diagnosed as epidermoid carcinoma, Grade III. An area measuring 8 by 10 inches was laid out over the temple and an adjoining area measuring 10 cm. on a side was laid out over the cheek. With this arrangement the irradiated region measured 20 cm. in its longest diameter. The two areas received 300 r on alternate days until each had been given 4,200 r. The factors were: 0.75 mm. copper and 1.0 mm. aluminum filter, 25 ma. and a 50 cm. target skin distance. Radium needles were implanted in the neck. At the end of three months all visible evidence of the carcinoma had disdisappeared but the ulcerated areas were replaced with painful patches of tough necrotic tissue which refused to heal and the patient eventually died of extension of his disease with little relief of symptoms.

Profiting from this experience a second case having an ulcerating carcinoma measuring 5½ inches in diameter on the left side of the face and head was treated with a less strenuous technique. An area measuring 15 cm. on a side was given a total dosage of 2,850 r during a period of nineteen days using factors identical with those adopted for Case v. All of the doses consisted of 300 r except three, and of these one was 250 r and two 200 r. This patient had a severe nephritis from which he died three months after he was treated but his relief from pain was immediate and at the time of his death all evidence of carcinoma had disappeared and the ulcer was reduced to half of its former size by normal epithelium growing over a smooth granulating surface from the wound edges.

From our experience with a filter of 0.75 mm. of copper and 1.0 mm. of aluminum we adopted doses of 4,200 r for areas 7 cm. in diameter; 3,600 r for areas 10 cm. in diameter; 3,000 r for areas 15 cm. in diameter, and 2,800 r for areas 20 cm. in diameter. Treatments were given daily but it was found wise to extend the total treatment time from two weeks to three weeks with the larger lesions utilizing smaller daily doses.

Merritt and Rathbone[8] have recently contended that large areas may be safely given as much as 4,500 r in twenty-five days when excessive filtration is utilized. With a filter equivalent to 5 mm. of copper and the other factors used by us, they have given such doses to areas measuring 20 cm. on a side and have obtained perfect skin healing. We are therefore increasing our total dosage delivered to large areas when the heavy Thoraeus filter (equivalent to 3.5 mm. of copper) is used but are not as yet in a position to give the largest safe dose that may be administered with it.

In some instances external irradiation does not produce a cure even when large doses and prolonged treatment periods are used. Quick[9] and Martin and McNattin[3] have shown how implanted radium or radon may be used to advantage in such cases to augment the total dosage. They have written for the most part about metastatic malignant glands in the neck and resistant tumors in the mouth in which it

has been found advantageous to insert gold radon seeds into resistant areas several weeks after the completion of the series of roentgen treatments. Since the implantation of weak platinum radium needles of the type advocated by us[2] into regions showing a radiation reaction is an unpleasant procedure for the patient, we have been interested in the use of these needles in advanced mouth and neck lesions prior to the application of the divided doses of roentgen rays. The needles are usually sewn into the tumor tissue in the mouth, lips and neck and left in place for seven days and roentgen therapy is started immediately after the needles are removed. Case VI illustrates the procedure.

Fig. 7. Epidermoid carcinoma, Grade III, involving the entire chin, mandible, floor of the mouth, right cheek and glands of the neck in a young man. Weak platinum radium needles were implanted in all accessible malignant tissue for seven days and 2,100 r was given to each side of the neck in fifteen days using a filter of 0.8 mm. of tin, 0.25 mm. of copper and 1.0 mm. of aluminum and an intensity of 15.6 r per minute. The epidermolysis was practically healed in three months as shown in the photograph on the right but the bone and neck are not clear of the disease. The roentgen-ray dosage should have been larger.

This patient had a hard mass of tumor tissue in the right cheek which measured about 1½ inches in thickness and 3 inches in diameter. The corner of the mouth was destroyed and carcinoma extended into the floor of the mouth and into the masseter muscle. There were no palpable glands felt in the neck. A piece of tissue removed from the tumor was diagnosed as epidermoid carcinoma, Grade I, a type which is thought to be radioresistant. Eleven 2.4 mg. platinum radium needles each having an active length of 4.0 cm. were sewn into the cheek and ten 1.33 mg. needles each having an active length of 2.0 cm. were sewn into the corner and floor of the mouth. At the end of a week the radium was removed and the right lower cheek and submental area was given 300 r daily through a 10 cm. portal until a total of 2,100 r had been given. The treatment factors were 220 kv., 2.0 mm. of copper and 1.0 mm. of aluminum filter and a target skin distance of 50 cm. At the end of two weeks both the inside and the outside of the cheek were denuded but the malignant tissue had completely disappeared. In three months healing was complete and function seemed good. Although the tumor may not be cured the palliation is certainly all that could be expected.

This case was so successful that several patients with advanced carcinoma of the jaws were treated with even more intensive techniques.

Case VII suffered from an epidermoid carcinoma, Grade III, which had originated in the lower lip. At the time of admission it involved all of the chin, the floor of the mouth under the tongue, parts of both cheeks, the midportion of the mandible and the submental glands. This was truly an unfavorable case since it occurred in a young man twenty-four years of

age. Fourteen 2.4 mg. radium needles having active lengths of 4.0 cm. were planted in the chin, neck and floor of the mouth and twelve 1.33 mg. needles having active lengths of 2.0 cm. were placed in the cheeks and remainder of the lip. At the end of a week they were removed and 300 r was given daily through 10 cm. ports alternately to the sides of the chin and neck until each side had received 2,100 r. The factors were 220 kv., 0.8 mm. of tin, 0.25 mm. of copper and 1.0 mm. of aluminum filter and a target skin distance of 50 cm. The reaction was rather severe but at the end of three months all visible evidence of the tumor has disappeared and the wound has almost completely healed leaving a big defect in the jaw. Some of the glands in the neck are still present but they feel soft and cystic. Needless to say, this patient's general condition is markedly improved. He is gaining weight and is no longer taking drugs for relief of pain. The results obtained indicate that the total roentgen dosage might have been safely increased to 3,000 r to each side of the neck with the factors used

Fig. 8. An epidermoid carcinoma of the lip was treated successfully with superficial roentgen rays six years before admission, as shown in the upper photographs. Glands appearing in the submental area five years later were large and inoperable at admission, as shown in the lower left photograph. Weak radium needles were implanted into and under the masses for seven days and 2,100 r was given to the submental area in seven days with the complete regression shown on the right. This improvement is of five months' duration.

by reducing the daily doses to 250 r. This patient will now be placed in the hands of a plastic surgeon but we cannot as yet forecast the ultimate result.

Quick has emphasized the value of a combination of radium and roentgen rays in treating metastatic carcinoma in glands of the neck. Case VIII is one which responded very well to our adaptation of this plan.

A carcinoma of the lower lip had been successfully treated in our office six years before admission with roentgen therapy. He remained well until a year before admission when he noticed two nodules growing beneath the chin. When he came to the hospital a hard, fixed, subcutaneous mass 1½ inches in diameter was felt in the midline in the submental area and a second node about ¾ inch in diameter was felt beneath the right mandible. Eleven 2.4 mg. platinum radium needles and five 1.33 mg. radium needles were planted under and around the glands for a period of seven days. During the same period of time 300 r was delivered daily to an area in the submental region measuring 15 cm. on a side until 2,100 r had been given. The factors were 220 kv., a filter of 2 mm. of copper and 1.0 mm. of aluminum and a target skin distance of 50 cm. A rather severe skin reaction appeared but it cleared up rapidly. The largest gland broke down rapidly and at the end of a month it had formed an abscess which was drained surgically. It contained much cheesy material. At the end of two months all evidence of the nodules was gone and the patient remains free of demonstrable carcinoma at the end of five months.

A word of warning relative to the use of large total dosages of roentgen rays over skin that has been previously irradiated may not be out of place. It has been our experience that cutaneous areas that have become tanned from the repeated application of erythema doses of high voltage roentgen rays given by the old massive dose technique respond very poorly to "modified Coutard" therapy with low filtration, and in certain instances reactions have occurred in which healing has been very slow indeed. It is therefore safest to restrict divided dose therapy to cases that have not been previously treated.

SUMMARY

Marked palliation and numerous cures can now be accomplished in advanced cancer about the head and neck by utilizing a modified Coutard roentgen technique with heavy filtration augmented at times by implanted radium.

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Vol. 36, No. 6

EIGHTEEN MONTHS' EXPERIENCE WITH 400 KV. CONSTANT POTENTIAL DEEP THERAPY*

A PRELIMINARY REPORT

By DAVID STEEL, M.D.
St. John's Hospital
CLEVELAND, OHIO

IN FEBRUARY, 1935, the St. John's Hospital of Cleveland installed, as part of their therapy department, a 400 kv. constant potential roentgen machine. At this time the literature on the use of voltage higher than the conventional 200 kv. was rather meager, yet there seemed to be enough to warrant at least the assumption that a definite advance had been made. It is the intention of this discussion to present in a general way my experience with this equipment, present a few cases, which all would grant readily have unusual features, present the technique and the factors used, and draw what conclusions seem to be justified conservatively at the present time.

Since installation the machine has been running at all times at 400 kv. constant potential, 5 ma., 80 cm. distance, and a constant filter composed of 0.93 mm. tin plus 0.27 mm. Cu plus an iometer chamber plus bakelite plus 3 mm. of copper built into the tube, giving a filter having the equivalent of 6.5 mm. of copper. The following is a report as presented by Dr. Otto Glasser under date of May 6, 1936:

General Electric 400 kv. Constant Potential X-Ray Machine.
Coolidge Tube XPT—4.

405 kv. sphere gap
5 ma.
204 primary meter
19 auto
23 rheo
80 cm. focal distance
Small treatment cone with bakelite bottom

I. Intensity with routine filter, i.e. iometer chamber—Thoraeus (0.93 mm. tin + 0.27 mm. Cu) + bakelite.
14.0 r/min.
(Same without iometer chamber in path of rays 15.2 r/min.)
Half-value layer for these conditions: 5.4 mm. copper

II. Absorption curve in tin

Filter:	r/min. in air (with iometer chamber)	r/min. in air (without iometer chamber)
2 mm. Cu (in tube)	20.5	22.9
2 mm. Cu (in tube) + 0.2 mm. Sn + 0.27 mm. Cu + 1 mm. Al	18.0	20.0
2 mm. Cu (in tube) + 0.4 mm. Sn + 0.27 mm. Cu + 1 mm. Al	16.6	18.3
2 mm. Cu (in tube) + 0.6 mm. Sn + 0.27 mm. Cu + 1 mm. Al	15.5	16.9
2 mm. Cu (in tube) + 0.8 mm. Sn + 0.27 mm. Cu + 1 mm. Al	14.5	15.7
2 mm. Cu (in tube) + 0.93 mm. Sn + 0.27 mm. Cu +	14.0	15.2
+1.0 mm. Sn + 0.27 mm. Cu + 1 mm. Al	13.6	14.8
+2.1 mm. Sn + 0.27 mm. Cu + 1 mm. Al	12.8	13.9

At the time of installation, I had had a limited experience with the protracted method of radiation therapy as proposed by Coutard and associates, and I felt that the clinical result in several cases was unusually good and far better than I had obtained with other methods. Believing that the method was basically sound, I immediately applied the general principles of protracted radiation to all cases treated on the 400 kv. constant potential machine. The daily dosage is low—seldom over 140 r, measured in air. As a rule two portals are used daily, and whenever possible the portals are so laid out as to crossfire the lesion and yet use any one single portal only once

* From the Department of Radiation Therapy, St. John's Hospital, Cleveland, Ohio.

every other day. This scheme is easily worked out in pelvic cases, breasts and almost all the common sites. The reactions, other than skin, are surprisingly minimal, the majority of patients going through the course with no serious complaint. Nausea and vomiting, so commonly seen with 200 kv., is rarely seen with the higher voltage, and these two symptoms are usually transitory, and as yet have not been severe enough to interfere completely with continuance of the course of treatment. Occasionally after the first few treatments a diarrhea develops, but at this stage it is always transitory and disappears without medication under further irradiation. Toward the end of the course diarrhea often returns, but is relatively mild, subsides with paregoric and stops readily after the treatments are over. Rectal tenesmus is practically never seen. The skin changes have the same clinical appearance as produced by 200 kv. except in the early stage. The erythema does not start as a general blush, but appears first as small dots, faint red and sharply defined, gradually growing darker and in a few days losing their identity in a generalized erythema. This erythema disappears much more readily than with 200 kv. therapy, leaving a skin soft and pliable, and only slightly decreased in moisture. The cosmetic result in large skin cancers is unusually good. To date no trophic ulcers have occurred and there has been no late skin change. No changes in the subcutaneous structures have been noticed and the subcutaneous fat has not undergone necrosis, even in the suprapubic areas in pendulous abdomens, in spite of the fact that high dosages have been administered, as will be seen in the case reports to follow.

In cancers of the female genital tract, urinary bladder and rectum, and to a less extent in other organs, the average patient shows an early response with a gradual return to well being, which at the end of the first week or ten days is quite apparent and continues throughout the course. There are a few, however, who will show this good reaction for a week or ten days and then will again begin to complain of a gradual increase of their original symptoms, and of a marked lassitude, loss of strength and appetite, dizziness, etc. It has been noticed many times that these patients have done very poorly and that the extent of the lesion, duration of the disease and the general physical condition are not necessarily an index to what patients will show this set-back. In the first few patients, therapy was continued in spite of these symptoms, but when it was realized that the patient showing this reaction steadily grew worse, not only was a poor prognosis given, but in many cases irradiation was discontinued. Then it was noticed that after a few days these symptoms again subsided and the patient once more began to feel better. At first it seemed almost hopeless to start again, but it was noticed that if these patients were given a rest period of several days, the irradiation could be continued without a recurrence of the symptoms and with a gradual return to well being. This chain of events has been seen in many cases and it is worthy of note that with the rest period the patient often does extremely well with further irradiation, whereas without the rest period and with continuation of irradiation in spite of the symptoms, the outlook becomes almost hopeless. As far as can be told to date no tumor has become resistant because of the delay or the protraction.

It is extremely important at the present time to curb enthusiasm with conservatism. It must be realized that the method I am using varies in several important ways from the method as commonly employed with 200 kv. I look upon the increase in voltage as a means to an end, and not as a figure of such magnitude as to offer a hope in itself of a great step forward. Figures are impressive, but are too often misleading and, as in several other fields of medicine, are all too often accepted as the final proof. Recent trends in therapy most certainly favor heavier filtration and even though further investigation might well prove that beyond a certain point added filtration is of

no clinical benefit, it seems to me at present that the heaviest filtration consistent with an economical r output is advisable. Such filtration gives us a shorter wave length and even though physical experiments on *Drosophilia* eggs, wheat seedlings and other test materials have all tended to prove that the biological reaction is independent of wave length, clinical experience makes one wonder whether these experimental conclusions are applicable to human tissue. This observation has recently been made by several authors in particular reference to 200 kv. therapy and it is borne out by experience with 400 kv. therapy. It would seem, therefore, that the increase in voltage gives us the opportunity of using heavier filtration with the resultant shorter wave.

A second important change coincident with the use of higher voltage is the application of the radiation according to the protracted method. I feel certain also that the shorter wave length, especially when used with the protracted method, affects the neoplasm more than the skin, and instead of having two structures: (1) the skin or the normal structures and (2) the neoplasm, reacting to about the same degree, as is the case with unfiltered or low-filtered radiation, we have two tissues one of which—the normal structures—reacts relatively little, and the other—the neoplasm—which shows in the majority of cases a well-marked reaction. This means that a much higher dose—a blistering reaction—can be given without fear of permanent damage to the normal tissue, resulting in a higher dose to the neoplasm, and yet a reaction which heals in a much shorter time than similar changes from lower filtration, leaving a skin difficult to tell from the normal or untreated surrounding areas, a difference which is more marked when large fields are treated, and particularly when cartilage is, or might be, involved.

At the present time I believe that the higher voltage, heavier filtration, shorter wave length, increased treatment distance, and the protracted method combine to make a great step forward in radiation therapy. It is naturally very difficult to evaluate what part each one of these factors is playing. Certainly eighteen months' experience is too short to draw conclusions as far as "cure" is concerned. I feel confident, however, that no one could go through the experience without being enthusiastic and certainly one is justified in saying positively that the clinical results are far better. I believe large tumors, especially of the urinary bladder and female pelvis, have responded to this form of therapy that would not have responded with other forms, and at the same time, only a very small percentage of the patients have experienced roentgen sickness, but on the contrary have shown rapid clinical improvement from the start.

Case 1. *Adenocarcinoma of the Body of the Uterus.*

This patient, Miss R. P., aged fifty-two, was referred by Dr. Leavenworth of Canton, Ohio, with the following note: "She came to me first in November, 1933, with the history of profuse menstrual periods for the past three years with numerous vaginal hemorrhages in between menses. At this time she was admitted to the local hospital where a biopsy showed a well-developed adenocarcinoma of the fundus. Radium was inserted, 100 mg. for forty-eight hours and the patient was discharged in about two weeks in good condition. She was advised to return in February for a hysterectomy but due to her father's illness she repeatedly postponed her operation and did not return for one year.

"In November, 1934, she returned and examination showed about the same condition with the exception that the mass had grown considerably. She was admitted into the hospital for a pan-hysterectomy. In separating the cervix from the bladder the tissue was very friable and there was considerable hemorrhage. The entire uterus tore away from the lower portion of the cervix, leaving a cervical stump and a large raw bleeding carcinomatous mass. At this time it was thought that the bladder wall was already invaded. The area was peritonealized as well as possible and the patient left the hospital in fair condition. She was advised to have deep therapy." Shortly after this the patient began to have hemorrhages again and

backache developed. This became so severe that the patient was not able to be up over five to ten minutes at any one time during the course of any one twenty-four hours.

She appeared for therapy on March 4, 1934, four years after the first symptom. At this time she had a large ulcerating mass in the region of the cervix which was bleeding profusely. She was given a daily dose of 140 r, measured in air, to two fields in front, giving a total of 2,240 r to each field and 1,360 r to each of two fields in back. By the end of this time the vaginal bleeding had entirely subsided and the backache had totally disappeared. She was completely free of her symptoms until the latter part of August when she had another hemorrhage and was returned again to see what could be done. Realizing that deep therapy was the court of last resort, it was explained to the patient the possible dangers of repeating the dose and she elected to go on.

We therefore resumed treatment and gave her an added dose of 2,380 r to each of the two fields in front and 2,240 r to each of two fields in back. These were measured in air. At the end of the treatment, the skin was slightly reddened and in about one week showed superficial denudation but no severe reaction. In spite of the relative heavy dose previously given, the second heavy dose did not seem to irritate the skin any more and what little change did take place healed readily. She has been seen off and on since this time and to date is completely free of symptoms. She has no backache and no bleeding and the vaginal vault is perfectly clear. There is no carcinoma to be seen.

We have, then, a case of adenocarcinoma of the uterus which was present four and a half years before roentgen therapy was started and which had been operated upon and had recurred. The case is of interest not only because of its duration, extent and cytology, but because of the fact that she is a patient that received two rather heavy doses of therapy into the same areas without showing any changes whatsoever residual in the skin. It further shows that the lesion did not become resistant to radiation, and it is this case that gave us the definite idea that irradiation could be repeated even though a heavy dose had been given. This is one of the early cases treated and since this time heavier radiation is given to the body of the uterus and cervix. Two fields front and two fields back are used and a dose of as near as possible to 3,000 r, measured in air, is given. Some patients have taken a heavier dose. In the average patient there is at the end of the course a well-marked epithelitis which subsides readily in about ten days and leaves no residual. Nausea and vomiting are very rare; tenesmus is practically absent and diarrhea, if present, is minimal and transitory. Those patients who show a progressive return to good health with minimal symptoms ascribable to irradiation have an excellent prognosis. In 62 cases of carcinoma of the uterus and cervix, no damage has been noted in the skin, subcutaneous structures, bladder or any part of the intestinal tract. It is too early to report these cases as a group except to say that the clinical disappearance of the malignancy is remarkable.

Case II. *Papillary Carcinoma of the Bladder.* Mr. L. E., aged fifty-one, referred by Dr. J. A. Sommer, who saw the patient first and demonstrated cystoscopically a tumor of the bladder about the size of a golf ball lying just above and a little to the right of the right ureteral orifice. Bleeding had been present for about six weeks, associated with frequency and loss of 15 pounds in two months. The urine was bloody and contained pus. Irradiation by 400 kv. constant potential was started on April 14 and was continued daily with the exception of Sunday until June 5. Four fields were used, two front and two back, each field receiving 140 r every other day. A total dose of 3,080 r was given to each anterior and 3,120 r to each posterior field. Bleeding stopped on about the tenth day and no other symptom developed. The skin front and back was mildly blistered but when seen three weeks after treatments were discontinued this had subsided completely. On July 24 the following note was received from Dr. Sommer, ". . . bladder capacity normal. Bladder neck normal. No diverticula. Ureteral orifice readily seen. The bladder mucosa is of normal pinkish hue throughout the entire viscus. There is no evidence of any new growth. The sight of the former growth is covered with normal mucosa.

Fig. 1. Case III. Before irradiation. Lesion of fourteen years' duration.

Fig. 2. Case III. Eight months after irradiation.

There is no evidence of any recurrence. The bladder is absolutely negative."

Case III. *Epithelioma.*

Mr. E. D., aged fifty-six, noticed a small "pimple" on the left nasolabial fold in 1922. Over the years it grew rapidly in spite of many varied local applications. At the time of the first treatment—November 23, 1935—the lesion (Fig. 1) extended from the right side of the bridge of the nose, across the bridge, below to about one-half the distance of the left eyeball, involving half of the upper lid and then downward toward the nasolabial fold and upward

Fig. 3. Case IV. Before irradiation.

Fig. 4. Case IV. Eight months after irradiation.

along the side of the nose to the bridge. The margins were raised and irregular and the eyelids eroded. The base of the lesion showed a serous discharge. The tear duct was completely eroded, and two large corneal ulcers were present. Because of cartilage involvement, the extent and duration of the disease and because it was thought the lesion would react to the shorter waves on the same basis as radium is used under such conditions and with the hope that surrounding structures would be relatively slightly involved with a reaction, he was treated with the higher voltage. He received a daily dose of 140 r, using one field, shielding the right eye with lead but making no attempt to protect the left eye. A total dose of 3,060 r, measured in air, was given. The lesion disappeared rapidly and shows no evidence of recurrence nine months later. The skin is in excellent condition, the corneal ulcers are healed, and the lens to date shows no changes and vision is normal. The lacrymal duct remains completely obliterated (Fig. 2).

Case iv. *Carcinoma of the Breast.*

Mrs. A. D., aged sixty-four, bruised her left breast three years and a half ago. In February, 1933, she noticed a small mass about the size of a hazelnut in the medial side. Irradiation was advised and she was given elsewhere 24 to 26 treatments, at the end of which time the patient stated her skin became very red. In about one year the mass was considerably larger and in November, 1934, it began to slough. Two weeks before I treated her, a biopsy showed a carcinoma simplex. At this time the entire right breast was also the site of a hard mass with all the clinical appearance of an advanced malignancy. The left breast in its medial half showed an area of ulceration (Fig. 3) 1 cm. deep and 4 cm. long by 2 cm. wide. A small gland was palpable in the left axilla.

The medial left breast, lateral breast, axilla and supraclavicular regions were irradiated. The medial and lateral breast each received 2,700 r and the axilla and supraclavicular fields 3,500 r, using two fields a day and giving 140 r to each field, measured in air. At the end of the course the skin was red, moist and slightly broken, but in spite of the previous irradiation with 200 kv. no alarming changes appeared and healing was rapid (Fig. 4). The breast ulceration completely healed. The right breast was then crossfired using a medial and lateral field, each portal receiving 2,450 r, one field and 140 r daily. The large mass entirely disappeared clinically. The lung fields to date show no fibrosis. It is interesting to note that the ulcerated area healed entirely after the irradiation with the higher voltage, that the tumor completely disappeared with this form of therapy, whereas it did not show such a reaction with the lower voltage and filtration, and that the skin, in spite of previous irradiation, healed in scheduled time and showed no unusual reaction.

In selecting the above cases it was quite natural to report the difficult or unusual case that did well, and it must not be assumed, nor is there any intention to intimate, that all the patients do as well. On many occasions, results have been quite disappointing, for it has been noticed many times that in spite of the best we can do, cases, which on the basis of previous experience would appear to be candidates for at least very successful palliation, have taken a steady downhill course, and in some of these it would also appear that irradiation played a very important, if not the only, factor in this course. Perhaps with more experience such unsuccessful cases can be recognized from the start, but at the present time there seems to be nothing else to do but treat by irradiation. I am beginning to believe that the action of radiation on the malignant cell is not the only response, but that there is another factor—as yet indefinite and unknown—which enters into the problem, making one case successful because of its presence, and another case unsuccessful because of its absence. As far as I am concerned, I believe without reservation that the use of higher voltage is a great step forward, but to assume without justification that the voltage factor alone is responsible is unwarranted. It is my experience that the factors of higher voltage with the use of greater filtration resulting in a shorter wave length, when used with the protracted method, combine to offer a great advance in radiation therapy.

Vol. 36, No. 6

DIRECT ROENTGEN IRRADIATION OF DEEP-SEATED TUMORS

PRELIMINARY REPORT

By SHERWOOD MOORE, M.D.

Professor of Radiology, Washington University School of Medicine, and Director of the Edward Mallinckrodt Institute of Radiology

ST. LOUIS, MISSOURI

THERE are two factors which determine the results of irradiation: the ability of tissue to respond to the absorption of this type of energy, and the quantity of energy delivered to the tissue. Though there is strong support of the view that the quality or wave length is the determinant of effect, it must be said that the burden of proof that such is the case rests on the proponents of this theory. Within limits, which are too narrow, the factor of amount of radiation delivered can be controlled. The other factor, capacity of response to irradiation, is governed by unknown causes and can be ascertained, if at all, only by trial. Perhaps in the future it may be discovered that radiation effects are solely a function of the energy absorbed. At present it is difficult to believe that this will ever prove to be entirely true. It is the experience of every radiotherapist that there are tumors that are affected not at all by any amount or quality of radiation.

The method of irradiation, which is to be described, was developed through trial and error over a long period. The two chief obstacles to the delivery of a suitable amount of roentgen radiation are the limitation of the apparatus and the location or depth of the area to be irradiated. A powerful deterrent to adequate treatment has been and is fear—fear of radiation burns with their frightful consequences both immediate and remote. This has accounted for many failures in roentgen therapy. Insufficient quantity of radiation delivered accounts for many more.

In order to overcome the power limitation of apparatus, to safeguard against burns, and to increase efficiency, I, in conjunction with Dr. V. P. Blair, carried out the following treatment in October, 1918: A case of intraoral cancer with extensive cervical metastasis was brought to the therapy room under anesthesia and, with the operative wound open and retracted, and without a dressing in place, was given a large dose of roentgen rays to the area where it was certain that all of the tumor had not been surgically removed. The patient was immediately returned to the operating room and the wound closed. The dose of roentgen radiation was 3 erythemas given with a mechanically rectified apparatus and 3 mm. Al filter. There was no interference with the healing of the wound or evidence of any injury to the exposed subcutaneous structures. This case has been reported by Blair and Brown.[1] After the above date this form of treatment was followed in similar cases sporadically until 1930. Experience with higher voltage apparatus and greater knowledge then warranted a more extensive trial of the principle.

Shortly after the date of the above treatment I was led to believe that modification of the method of treatment of skin cancer then used would bring about better results. The practice in this type of case was to administer a series of small doses, usually an erythema, at varying intervals over a long period. In addition to the uncertainties of this method of treatment it seemed that some of the skin cancers became refractory, and their bases became fibrotic and the skin margins burned. Experiment with increase of dose and decrease of filter and fewer treatments gave better results. There was, however, always present the fear of roentgen burns. This was overcome

A *B*

Fig. 1. Washington University Clinic No. A 94086. April 11, 1923, patient given 8 erythema doses, no filter, approximately 70 kv. *A*. Before treatment. *B*. Two months later. Note perfect healing of marginal skin burns.

through the observation that radium burns of the skin could readily be cured by excision and plastic repair. The low intensity of radium used in this type of case limited the area of the burn. Therefore, if a roentgen burn were so limited, little or nothing need be feared as it could be satisfactorily treated. Consequently, larger and larger doses of roentgen radiation were given to skin cancers with decrease of filter until finally no filter was employed, always with betterment of the final result. It was found that one application of 8 or more erythema doses in the average case resulted in prompt and permanent disappearance of the lesions (Fig. 1). This method has been continued to the present time (Figs. 2 and 3), and, in addition to proving satisfactory, no ill results from excessive doses have occurred. However, care was exercised to see that no area too large for excision and repair was produced, should adverse effects follow the treatment.

The following lessons were learned from treatment of skin cancer and tumor exposed through an open wound.

A *B*

Fig. 2. B. H. No. 111510. Patient given 5,180 r at 85 kv., no filter, supplemented by 600 r, 200 kv., 0.5 mm. Cu plus 1 mm. Al filter because of the deep nature of the lesion. *A*. Before treatment. *B*. Appearance sixty-seven days later. Biopsy of margin of ulcer showed no evidence of carcinoma. Note recovery of skin from roentgen reaction.

1. Enormous doses of roentgen radiation could be safely given to cancer of the skin at one sitting.

2. The surrounding skin margin of such a lesion, though suffering a burn, resulted in neither immediate nor late ill effects.

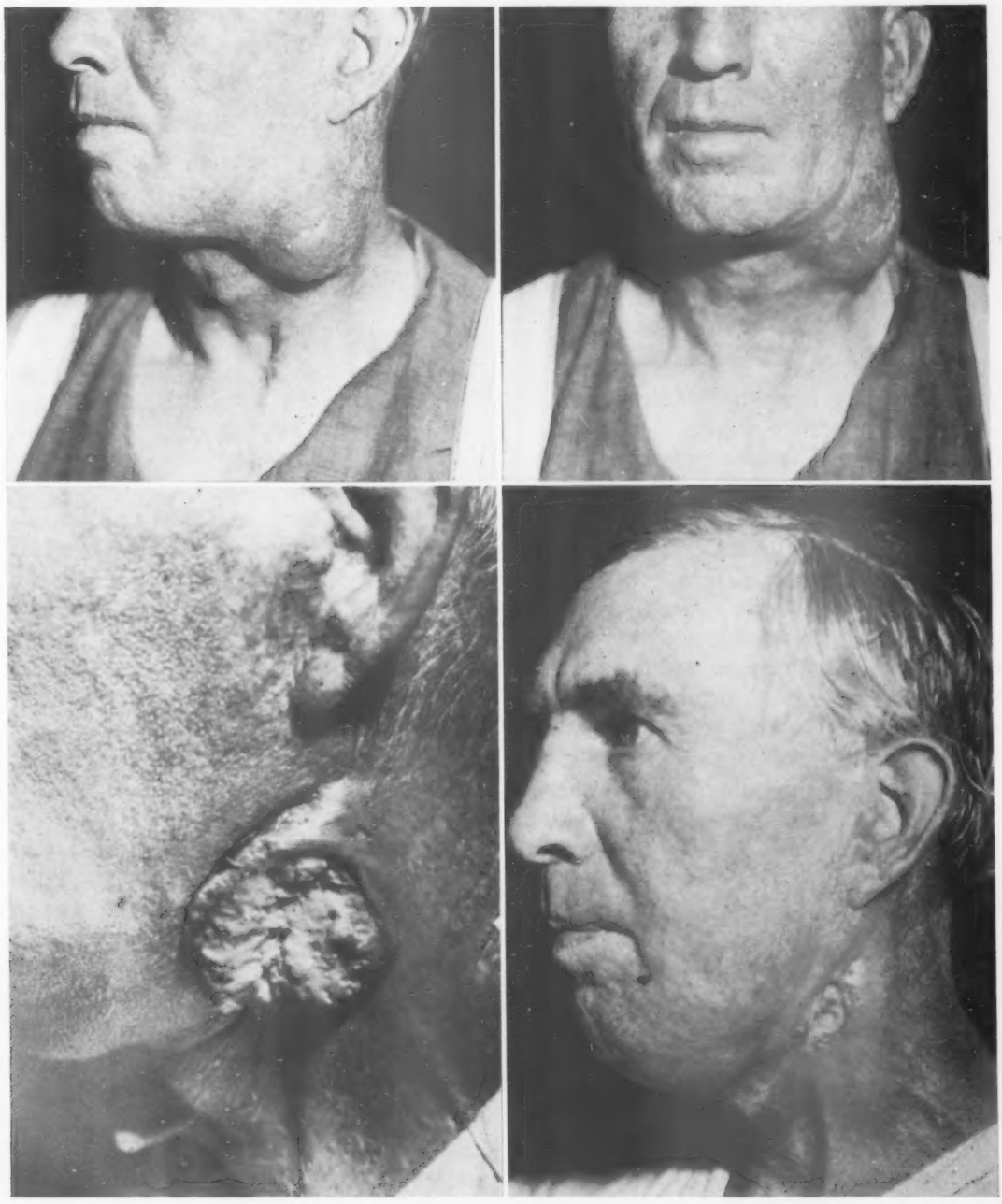


Fig. 3. B. H. No. 108969. Patient with extensive squamous carcinoma, floor of mouth. Radon implantation to primary lesion. A total of 5,050 r (measured in air) delivered in daily equal fractions to neck, between November 22, and December 18, 1935, 200 kv., 0.5 mm. Cu plus 1 Al. Left below: close up view of cervical metastasis, June 22, 1936. June 23, 5,000 r (measured in air), 85 kv., 0.5 mm. Cu plus 1 Al. Right below: lesion August 11, 1936.

3. With low voltage no ill effect in deeper normal structures followed.

4. It is safe and desirable to give any amount of roentgen radiation if it is absorbed by tumor tissue.

5. That there was ground for the belief that if low voltage, unfiltered roentgen rays could be delivered to deep-seated tumors, results comparable to those obtained at the body surface might follow regardless of the different natures of the tumors.

Excessive amounts of roentgen radiation cause fibrosis of many tissues and occasionally so alter bone as to make it fragile. However, only in the case of skin and possibly mucous membranes does late malignant disease occur. Consequently it may be said that radiation carcinoma is confined to the skin, and that excessive roentgen irradiation of subcutaneous structures is free from the hazard of late malignancy. This is in contrast with radium. Occasionally sarcoma follows chronic radium intoxication, and also its therapeutic use. Deleterious effects from either source are more likely to occur on repeated applications, and the risk of producing them is less, the fewer the number of exposures.

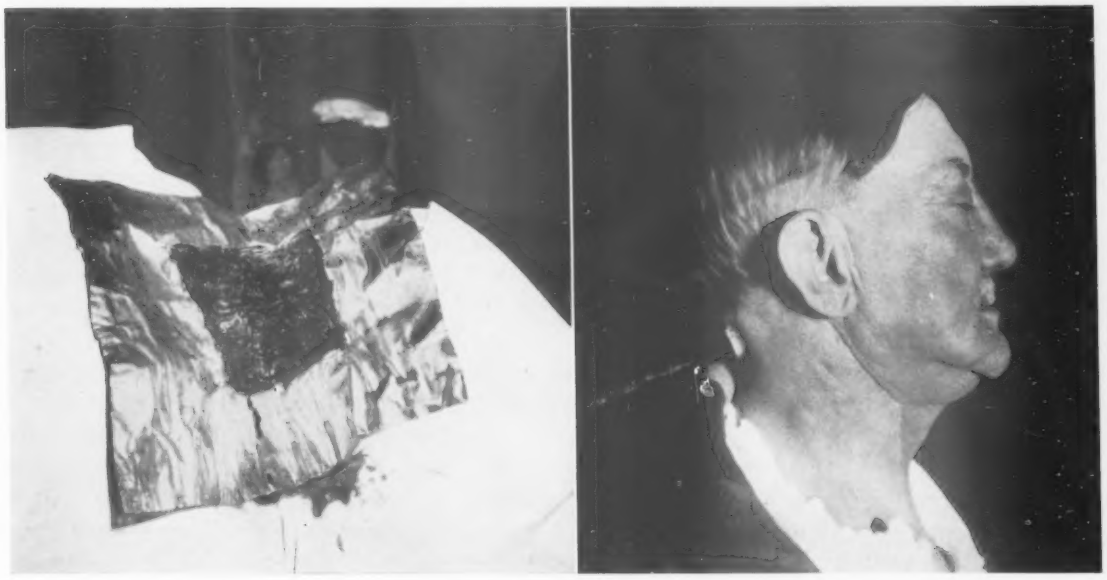
From the case of the first treatment through the open wound and the experience with superficial treatments, a plan of attack by irradiation on suitable cases of deep-seated malignant disease was formulated. "Suitable cases" are defined as those in an advanced stage, surgically inoperable, too extensive for radium implantation, which by trial have been found refractory to external roentgen irradiation, are free from remote metastasis, or which for any other reason are considered unsuitable for usual methods of therapy.

Roentgen irradiation through the open wound with or without neck dissection, or more or less complete removal of the growth in or adjacent to the buccal cavity, has been the field in which there has been the greatest experience. At first, the cases were treated with high voltage (200 kv. (constant potential)), relatively heavy filtration (1 or 0.5 mm. Cu plus 1 mm. Al) and relatively low r input. The patients were treated immediately after operation, and anesthesia was continued in the treatment room with avertin. Following the roentgen treatment the patients were returned to the operating room for wound closure. Due to the loss of anesthetic effect, patients became restless and moved too much for the safe administration of the quantity of radiation desired. In consequence the dose given in the early cases was frequently less than had been intended. The procedure has been changed, and the treatment of the open wound is deferred until the patient has recovered sufficiently from the anesthetic to be instructed to remain quiet. Sometimes the treatment, depending on the type of anesthetic used, is deferred to the day following operation. This delay, so far, has had no effect on the healing of the wound (see Figs. 4 and 7).

Surgical details of this method of roentgen treatment will be omitted as the cases will, in due course, be reported by others. However, mention of a few points are in order. Reflection of the tissues overlying the area to be treated should be extensive enough to permit exposure of all the involved or suspected area. The reflected flaps should be sutured in place. Lead foil 1 mm. thick should slightly overlap the flap margin and extend outwardly sufficiently to protect the skin from both direct and scattered radiation, and be securely sutured in place (Fig. 4). If voltages of 160 kv. or over are employed, rubber dam should be placed between the lead foil and the flaps. This will absorb the irritating secondary rays arising from the lead.

As experience has grown, I have concluded that better results follow the use of lower voltages, minimal or no filtration, and greater r output. Voltage and filter should be determined by what is estimated to be the depth to which radiation effect is desired. Fixed routine of voltage and filter should not be followed but should be adjusted to the individual case.

At present no statement as to the value



A *B*

Fig. 4. B. H. No. 94245. *A*. Illustrating field to be irradiated and arrangement of lead. *B*. Illustrating healing of reflected flaps.

of this method of treatment of metastatic carcinoma of the neck can be made. All cases were far advanced with a virtually hopeless outlook from any form of treatment, and several pursued an unmodified course to the usual terminus of the disease. However, I believe that certain points have been established. A new and radical method of attack has been applied to advanced and hopeless cases of carcinoma of the neck in which conventional methods of treatment promise little or nothing. The surgery employed has been of almost trivial consequence to the patient. There have been, so far, no immediate ill effects from either the surgery or the irradiation, nor, indeed, have there been any late disturbances. Even the roentgen sickness to be anticipated from a comparable dose of roentgen rays given under other conditions has been lacking, a fact that corroborates my opinion that this troublesome complication is, in large part, traceable to the action of roentgen radiation on the skin.

In addition to the 27 cases of carcinoma of the neck, 2 cases of metastases to the axilla from cancer of the breast were treated with the same method and with like result.

If the head and arm are suitably placed, the structures of the neck and axillary space will be approximately flattened out. This is important in roentgen therapy of these regions as a more uniform intensity of radiation is distributed than would be the case otherwise. In this way the physical conditions prevailing in the treatment of cancer of the skin, in which the best results

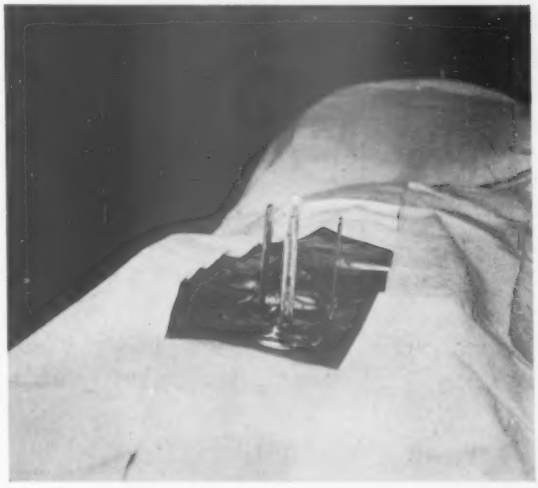


Fig. 5. B. H. No. 96873. Rose retractor in position, protective lead in place. Patient prepared for treatment.

are seen, are approximated. When using an agent which follows the rigid mathematical rules that roentgen radiation does, physical considerations undoubtedly have much to do in determining success or failure in radiation therapy.

It occurred to me that direct irradiation might be advantageously applied to a hollow viscus if it were made accessible and flattened. Advanced carcinoma of the base of the urinary bladder is one of the most disappointing in its response of all the malignancies that the radiotherapist is called on to treat. Through the interest of Dr. D. K. Rose, Assistant Professor of Genito-Urinary Surgery, Washington University School of Medicine, a suitable case was treated on the principle applied in the neck cases on May 5, 1934. In order to secure exposure of the lesion and to flatten the bladder, Rose devised a special retractor (Fig. 5). This instrument and its application have been described.[2]

In treating cases of carcinoma of the urinary bladder, 5 in number, it was found that it was necessary to keep the patient anesthetized during the roentgen treatment. In the first patient this limited the dose to 1,900 r, the other factors being 85 kv. (constant potential), no filter. The cystostomy wound closed in three weeks, and at the end of six weeks, cystoscopic examination revealed no evidence of the presence of tumor and there was complete healing of its site. This patient was discharged from the hospital symptom-free, but died some months later in another locality from some cause, so far as could be determined not associated with the bladder tumor or its treatment. Of the 4 other cases of tumor of the bladder treated by this method statements as to only one can be made. This patient died several months later, and, at autopsy, massive intrapelvic extension of the tumor was present. No trace of tumor, grossly or microscopically, could be found either at the site of the primary lesion or in the underlying bladder wall. It is noteworthy that these patients suffered none of the ill effects that would be anticipated from so radical a procedure. There was no spasm, no contraction, no hemorrhage, and an unusually prompt closure of the cystostomy wound. I believe that the absence of spasm and contracture is to be attributed to the fact that the bladder musculature was unaffected because of the low penetration of the rays used. The complete absence of any rectal symptoms in all cases is also explained in this way. Since this method of treating carcinoma of the bladder requires the opening and flattening of that organ, it can be applied only to tumors of its base.

As these cases are to be reported elsewhere by others, further comment will be refrained from except to say that in 2 of the cases, the disappearance of the vesicle lesion was dramatic in its promptness.

Five examples of extensive bronchogenic carcinoma from the service of Doctors Graham and Singer have been treated through an open wound. In 4 of these, the treatment was given through the thoracic wall after reflection of the superficial tissues overlying the tumor, the surgical procedure in all being identical in principle with that followed in the neck cases. In Case 3 in Table 1 the treatment followed a right lower lobectomy because of the impossibility of removal of an extensive mass of malignant tissue at the hilus of the lung. The roentgen radiation was delivered through the thoracotomy wound which, though not large, sufficed, through the divergence of the beam of rays, adequately to cover all of the suspected area. The margins of the thoracic opening were protected with lead foil. Bronchoscopic implantation of radon into the stump of the bronchus was later done. The patient was discharged from the hospital free from any bronchoscopic evidence of remaining tumor. Regression of the tumor in this case was prompt and most gratifying. Unfortunately, this patient died at home within a short time of a spinal or spinal cord metastasis. The 4 tumors of the lung treated through the thoracic wall yielded no immediate detectable response. However,

TABLE I

ROENTGEN THERAPY THROUGH THE OPEN WOUND

Cases Treated May, 1933, to August, 1936

Patient's Hospital Number	Dose (Roentgens Measured in Air)	Date
Metastatic Carcinoma of the Neck from the Buccal Cavity and Adjacent Structures		
1. B. H. No. 90349	1000	5-27-33
2. B. H. No. 90588	2120 (Two areas exposed)	6-12-33
	2025	8-24-33
3. B. H. No. 90760	1320	6-26-33
	2025 (Repeated dose)	8-24-33
4. B. H. No. 91887	2610	8-15-33
5. B. H. No. 92854	2385	10- 4-33
6. B. H. No. 93961	2535	11- 1-33
7. B. H. No. 76702 (Patient dead)	3600	11-10-33
8. B. H. No. 94245	3900 (Right side)	12-14-33
	2475 (Left side)	2- 1-34
9. B. H. No. 90596	3006	1-19-34
10. B. H. No. 91118	4815	1-25-34
11. B. H. No. 94989 (Dead)	4280	1-26-34
12. B. H. No. 96311	3948	4-11-34
13. B. H. No. 97425	5978	6- 6-34
14. B. H. No. 97415 (Dead)	1976 (Left side)	6- 8-34
	1129 (Right side)	
15. B. H. No. 100735	4020	6-11-34
16. B. H. No. 97766	2100	6-22-34
17. B. H. No. 98859	1980 (To each side)	8- 7-34
18. B. H. No. 98979 (Dead)	1984 (To each side) Through the flaps	8-17-34
	640 (To each side) Through the flaps	11-28-34
19. B. H. No. 94471	4020	10-29-34
20. B. H. No. 100924	4020	11-12-34
21. B. H. No. 96703	2162	11-27-34
22. B. H. No. 101515	4020	12- 8-34
23. B. H. No. 103479	4000	3-16-35
24. B. H. No. 104096	4984	4-10-35
25. B. H. No. 103275	4984	4-20-35
26. B. H. No. 107132	4000	5- 6-35
Total Neck Cases		26
Tumor of Axilla		
27. B. H. No. 90884	1350	6-24-33
28. B. H. No. 102179	4028	1-16-35
29. B. H. No. 113868	4000	5-29-36
Total—Tumor of Axilla		3
Carcinoma of Urinary Bladder		
30. B. H. No. 96873 (Dead)	1926	5-15-34
31. B. H. No. 103361 (Dead)	2482	3-12-35
	3010 (Repeated dose)	5-21-35
32. B. H. No. 106384	1500	7-17-35
33. B. H. No. 10782	1500	9-18-35
Total Bladder Cases		4

Table I (*Continued*)

Patient's Hospital Number	Dose (Roentgens Measured in Air)	Date
	Carcinoma of Lung	
34. B. H. No. 45322 (Dead)	4180	2-20-35
35. B. H. No. 47033	5000	4-24-35
36. B. H. No. 45805	4240 (2120 each day)	10-29 & 30-35
37. B. H. No. 43780	4150	2- 5-36
38. B. H. No. 52984	5000	7- 6-36
Total Lung Cases		5
	Carcinoma of Rectum	
39. B. H. No. 111660	4000	4-13-36
Total Rectal Cases		1
	Brain Tumors	
40. B. H. No. 95070	4000	5-25-36
41. St. Louis Children's Hospital No. M. 1402	2500	8- 3-36
42. B. H. No. 116074	4000	8-24-36
Total Brain Cases		3
Grand Total		42

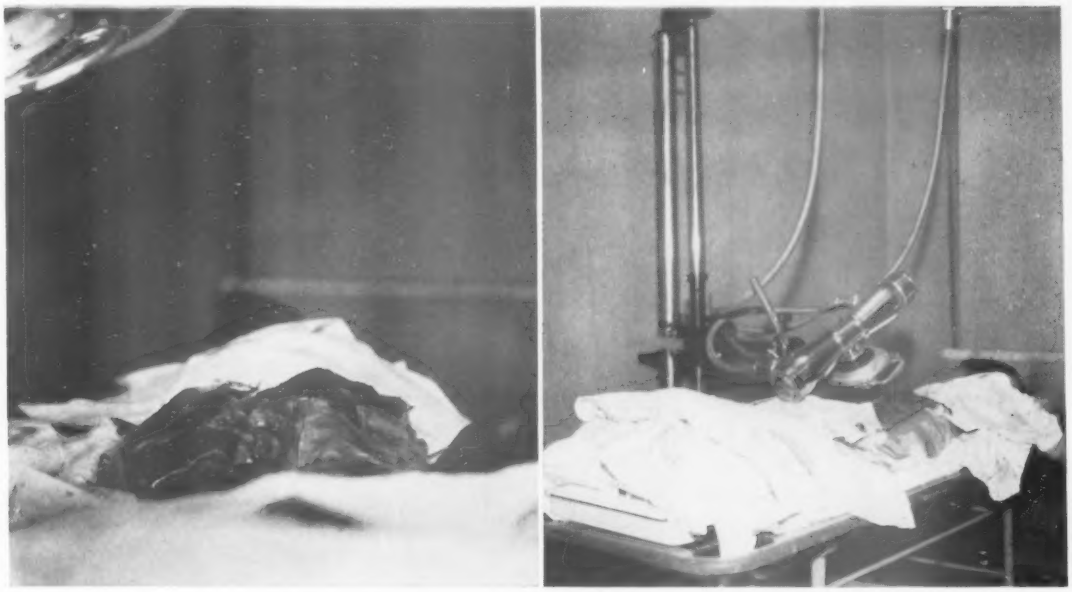
atelectasis may have masked any regression that may have followed the treatment. The lung cases were equally free, with those of the neck, from any immediate untoward result either surgical or radiological. Conclusions on the value of the method will be reported later.

An extensive rectal carcinoma, service of Dr. Warren Rainey, was treated by this method following a Kraske operation and incomplete cautery destruction of the tumor mass. There were no following complications (Fig. 6).

In uterine cases the combined use of radium and roentgen radiation has been so satisfactory that there was no reason to believe that a greater quantity of radiation would have improved results. Consequently direct tumor irradiation has not been attempted in uterine cases.

Brain tumors remain localized except for the migration by continuity of tissue of medulloblastoma. They should therefore, because of the absence of remote metastasis, be the most favorable class of neoplasms for radiation therapy. This has been far from the case, though remission of symptoms, of greater or less duration, is the rule in irradiated brain tumors. In time the remissions become shorter and less in degree. Nevertheless I believe that all cases of inoperable or partially operable brain tumors should be irradiated, provided there is a definite histological diagnosis, and recurrence is feared, and I have put the belief into practice. However, the results have not been equal to those obtained in other tumors. My results of roentgen treatment in a series of brain tumors have been reported by Sachs, Rubinstein, and Arneson.[3] I am of the opinion that had larger dosage been employed, more benefit would have ensued. Fear of severe scalp, or calvarial injury, especially of osteoplastic flaps, and meningeal trauma, has been a powerful deterrent to intense irradiation of brain tumors.

Three cases from the Neuro-Surgical



A *B*

Fig. 6. B. H. No. 111660. *A*. Rectal case in position. Note that a sheet of lead foil on patient's right side has shifted. *B*. Therapy tube of low voltage apparatus in place. This represents the ideal apparatus except for low milliamperage.

Service of Doctors Ernest Sachs and Leonard Furlow have been treated through the open wound. The first of these was a postoperative recurrent cerebellar medulloblastoma. This case was extremely refractory to external irradiation, receiving only temporary benefit. Following his first operation, six series of treatments in twenty-four months, with a total of 12,378 r, were given to the cerebrospinal axis. The risk of endangering the scalp and calvaria was too great to justify additional external irradiation. On May 6, 1936, Dr. Sachs reopened the old cerebellar craniotomy and removed as much of the recurrent tumor as possible. Following the principle of protection of the wound margins as in other cases and with special safeguards against infection through suitable dressing over the craniotomy, the patient, under avertin, was taken to the roentgen therapy room and given 4,000 r (160 kv. (constant potential), 0.25 mm. Cu filter). Wound closure immediately followed. The patient had an uneventful, undisturbed postoperative course (Fig. 7).

The second intracranial case was also a postoperative recurrent medulloblastoma arising from the floor of the fourth ventricle which responded but little to 8 series of external irradiation in twenty-six

Fig. 7. B. H. No. 95070. Illustrating complete healing of scalp in brain case.

months for a total of 13,882 r to the cerebrospinal axis. Re-operation and removal of tumor was followed by a dose of 2,500 r administered through the open craniotomy with identical methods and results as in the first case. The third case of brain tumor (still in the hospital at the time of writing) was a large spongioblastoma multiforme of the right temporal lobe which had been operated on and irradiated elsewhere. Because of its large size, and its infiltrating nature, the surgical removal of the tumor could scarcely be thought to be complete. It received 4,000 r through a craniotomy. Doctors Sachs and Furlow are to report these cases in detail at a date which will permit evaluation of the ultimate results of this method of treatment.

The cases treated through the open wound have been arranged in chronological and regional order in Table 1.

It will be seen from the table that, as experience has grown, the dose has increased progressively. I am convinced that the smaller doses are relatively useless. I believe that the optimum dose has not yet been determined, but that it is at a higher figure than any contained in the table. These doses have been limited by the duration of the anesthetic, when one was used, and the ability of the patient to remain quiet in one position for the necessary length of time, occasionally an hour and forty minutes.

Size of dose and method of administration have to be determined in large measure by the apparatus available for this method of treatment. Two types of equipment (both of constant potential and shock proof) have been used: one with a maximum of 135 kv. and 3 ma. which can be used without a filter, and the other 200 kv., 15 ma. which, because of the nature of its construction, cannot be operated at less than 160 kv. and with a filtration of the value of 0.25 mm. Cu. The former apparatus is a little more difficult to adjust to the area to be irradiated but is, except for the length of time required to give the necessary treatment, more desirable. It has been found that 85 kv. and no filter give the best results. Whenever conditions permit, unfiltered low voltage rays are therefore preferred.

The ideal apparatus would be one with which large output of radiation is combined with a wide voltage range and filter adjustable from zero to say 0.25 mm. Cu. In such an apparatus insulation and cooling of the roentgen tube would be a great problem. I believe that if the value of this method of treatment should be established, suitable apparatus would have to be designed for the purpose and used in the surgical operating room.

It has been stated above that insufficient dosage accounts for many radiotherapeutic failures. This has always been known and radiotherapists have evolved many ways to surmount this obstacle. Among these are the development of the hot cathode tube, higher voltage apparatus, increase of filter, radium and radon implantation, and the technique of the "cross fire."

The latest and most widely used advance in roentgen irradiation is the prolonged, fractionated dose method developed by Coutard. This is in contrast to the procedure, which it has largely superseded, of a large, single dose repeated at intervals. Treatment by the Coutard method permits the final administration of a larger quantity of roentgen radiation but it is not to be supposed that it is established as a fact that, given a like quantity of radiation, it is superior to a single large dose. This is true in spite of the fact that the former method is based on the theory that frequent application will be absorbed when cells are in process of division and hence are more vulnerable.

Roentgen-ray doses repeated on the skin are fraught with many dangerous possibilities, chief of which is the development of late so-called roentgen cancer. Though this occasionally follows a single, excessive roentgen-ray exposure, the likelihood of its production increases greatly with the number of exposures. I have observed this occurrence with a fatal outcome nearly thirty

years after the roentgen treatments were discontinued.

In view of this danger it appears that if like results can be obtained, the "single massive dose" should be preferred to the repeated, fractionated dose of radiation.

Probably the lower life expectancy of the "cancer age" and the high mortality of cancer have saved the radiotherapist from a harvest of late irradiation disasters.

There are certain points regarding the relative merits of the "single massive dose" and the fractionated dose of roentgen radiation which should be recalled. Before the advent of the hot cathode tube, excellent results (confined chiefly to superficial lesions, it is true) followed the administration of the small repeated doses which were only possible because of the limitations of the gas tube. Owing to the great advances in design of apparatus and tubes, this fact is generally overlooked. It should also be remembered that the radium pack, radon implantation, radium element application, e.g., as in uterus, are, in point of fact, "single massive doses" and also that it is in this field that more and better results are secured.

I am unfamiliar with the low voltage contact therapy of Chaoul. However, the method which has been described above seems to embody the identical principle and at the same time to be free from the inflexibility both as to voltage and limitation of portal size inherent in the Chaoul apparatus.

In concluding this preliminary report, I am of the opinion that the method of treating carcinoma which has been described has, except for cancer of the skin, shown little of curative value. However, the absence of such evidence does not nullify the fact that the method is an advance in fulfilling the quantitative factor necessary in radiation therapy under the hypothesis which I have formed.

On the other hand, the method has been free from injurious results to the patients and has in some cases resulted in remarkable amelioration of the patient's condition. The surgery of exposing deep-seated lesions has been entirely free from ill effects.

The quantity of roentgen radiation administered has been decided upon empirically, the determinants being in the early cases fear of the effects of a large dose, and in the later ones the limitation imposed by anesthetic and apparatus. It is proposed in the future to administer larger amounts of low voltage unfiltered radiation. Until experience has been gained with this type of radiation, the real value of direct roentgen irradiation of tumors cannot be determined. Enough has been gained, however, to justify further trial.*

I wish to express my appreciation of the high privilege of collaborating in this work with Drs. V. P. Blair, J. B. Brown, N. A. Womack, D. K. Rose, E. A. Graham, J. J. Singer, E. Sachs and L. T. Furlow.

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* This paper was just concluded when a spongioblastoma multiforme was treated through the open craniotomy. The dose was 5,600 r (measured in air), 160 kv. (constant potential), 0.25 mm. Cu filter. Description with photographs will be published by Drs. Sachs and Furlow.

PLASMA CELL MYELOMA OF THE HUMERUS TREATED BY ROENTGEN RADIATION

REPORT OF A CASE FOLLOWED SEVEN YEARS

By CORNELIUS O. BAILEY, M.D.
LOS ANGELES, CALIFORNIA

The patient, G. T., was a male, aged sixty-five, lawyer, residing in Texas. He was admitted to St. Paul Hospital, Dallas, July 8, 1929, for observation because of pain in the right arm. He was in excellent general physical condition, weight 196 pounds.

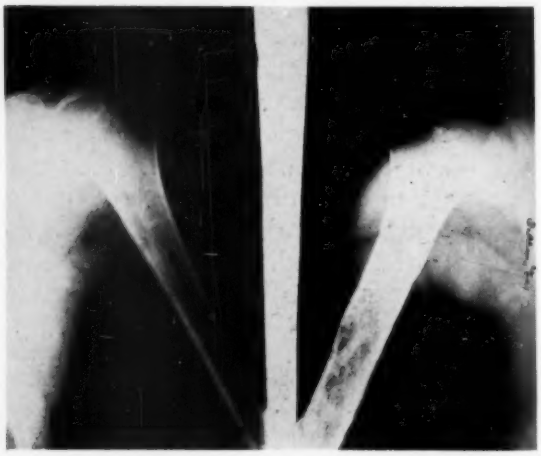

FIG. 1

History. Ten years ago the patient fell through a trap-door of a barn, with stretching injury to right shoulder region. Apparent healing, with normal function followed, and the patient was in excellent general health until one year ago when he noticed slight rheumatic pain in the right arm, near the shoulder. Massage gave no relief. Five months ago he noticed that pain was becoming progressively worse. Thinking the pain to be of rheumatic type, he used the arm extensively, hoping to "work it out," but without success. Two months ago the pain became so severe that he consulted his physician. Pain occurred on movement of the arm but function was not actually impaired or restricted until about six weeks ago.

Blood count was essentially normal. Urine examination negative. No Bence-Jones protein. Wassermann and Meinicke reactions negative.

Roentgen examination at that time was reported as probably osteomyelitis (Fig. 1). A trocar was inserted into the humerus and material obtained for microscopic examination and culture; no bacteria were demonstrable in the direct smears. Cultures remained sterile after forty-eight hours. On July 27, the patient was admitted to the hospital and the humerus was trephined and material taken for bacteriological study, which was reported negative after forty-eight hours. During this time, his condition was becoming progressively worse. He was no longer able to use his arm and his suffering was intense.

Patient's condition became decidedly worse and he was readmitted to the hospital on August 26, at which time the provisional diagnosis was still osteomyelitis. Biopsy was done the same day and sequestra of bone removed for microscopic study. At this time the blood

FIG. 2

count was essentially normal, as was the urine analysis. Roentgen examination revealed a marked extension of the process with a pathological fracture of the upper third of the right

humerus (Fig. 2). Temperature remained essentially normal throughout the entire illness. On August 29, the urine showed a heavy trace of albumin. On September 7 there was a trace of albumin but protein was not demonstrable and no Bence-Jones bodies were found at any time. On August 29 the cultures were reported sterile. Examination of tissue by Dr. J. L. Goforth was reported as follows:

Microscopic Examination. The sections show a very cellular neoplasm composed of rather small, round cells, which have prominent, deeply staining rounded nuclei and relatively scanty neutrophil cytoplasm. The nucleoli are prominent, many cells are in mitosis. The cells do not form structures as they grow, but here and there a sort of alveolar arrangement is assumed, and in other places, they tend to grow in colums. Elsewhere the cells seem to grow along thin fibrous trabeculae, as though they were surfacing it. In places the cells are entirely discrete; in others, especially in the column patterns, the cytoplasm almost fuses with that of its neighbor. Growth

Fig. 3

of the tumor cells appears to be rapid, and individual cell invasion occurs at will, even in the fibrous areas.

Dr. Goforth reported this as malignant and resembling myeloma and the tissues were referred to Dr. James Ewing of New York City. Dr. Ewing reported as follows:

It would seem that there were changes in the bone, going on for ten years, probably of the nature originally of a low grade osteomyelitis. The roentgenograms show an extensive honeycombing of nearly the whole of the shaft of humerus and I have no doubt that the whole bone is involved. I see no indications of involvement of the other bones in the

Fig. 4

roentgenograms, but a lesion so extensive suggests a search for other bone tumors. It also has a bearing on the question of operation. If other bones are involved, there is no use amputating.

The histological sections are quite puzzling. I think first of a metastatic carcinoma, since there is a certain alveolar arrangement. I would hunt for primary tumors in other parts of the body, but I do not think you will find any. After careful study, I have come to the conclusion that you have to deal with a plasma cell myeloma. In some places the cells have distinct plasma cell characters, but most of the cells are larger with more cytoplasm, which might be expected in a neoplastic plasma cell. The urine should be examined for Bence-Jones protein, which is present in some, but not all cases of plasma cell myeloma.

As to treatment, I doubt if amputating will be of any real service. Full doses of roentgen rays, high voltage, two or more erythema doses delivered within two or three weeks, may very well cause the disappearance of the lesion of the humerus. This tumor is generally quite radiosensitive. The outcome will

Fig. 5.

then depend on secondary deposits, which I think you must expect and be prepared to treat as they arise. I do not think the tumor is an endothelial myeloma. No cases of this disease have been observed at this late age. Of course, if the tumor does not respond to irradiation, and the pain and disability in the arm is not relieved, then amputation must be considered, but I do not think amputation can be regarded as curative.

Patient received 2½ erythema doses of aluminum-filtered 140 kv. roentgen therapy over a period of two weeks, divided into twelve doses. Six weeks later 3 skin units of the same type of radiation were given. After the first series of treatments all pain and discomfort disappeared and roentgenograms showed definite evidence of healing (Fig. 3). Roentgen examinations made during the six months following treatment showed a rapid deposition of lime salts and the bone rapidly assuming normal form (Fig. 4). Roentgen examination made August 3, 1936, revealed the condition unchanged over a period of six years and there is no definite evidence of disease (Fig. 5). Clinically, the patient is in excellent condition seven years later.

Acknowledgment is made to Drs. Samuel E. Milliken and N. B. Beaver of Dallas for their cooperation in treating and following this case.

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A REVIEW OF PRELIMINARY RESEARCH UPON THE COMBINED EFFECTS OF FEVER AND ROENTGEN RADIATION UPON ANIMAL TUMORS*

By STAFFORD L. WARREN, M.D.
ROCHESTER, NEW YORK

A STUDY of the effect of roentgen radiation alone and when used in combination with an elevated body temperature upon animal tumors is accompanied by the difficulty that such experiments must be done upon a statistical basis and the probability that a direct comparison with the effects of similar radiation upon human tumors is not possible. However, it is probable that some of the basic principles concerned in the effects of radiation upon tumor tissues and normal structures can be elaborated in such a manner as to allow a direct attack upon the tumor problem in human beings. The present review concerns the work done by various research fellows in the Division of Radiology in collaborative studies of some considerable duration and extent.† The details of these studies will be published elsewhere.

There has been a great deal of speculation regarding the amount of radiation necessary in one massive dose to kill a mass of tumor cells completely either in vitro or in situ in vivo. Clinical experience has pointed out the fact that it is almost impossible to destroy deep-seated tumors by the massive dose technique without simultaneously causing irreparable damage to the nearby normal tissues. It seems logical to attempt to work out the lethal amounts of roentgen radiation and radiant energy (in the form of heat) which might destroy tumor tissues in the animal body with the hope that by varying the time and dosage relationships a way might be found around this impasse. In a measure, this might suggest to what extent a similar principle might be applied in the treatment schedules in tumor clinics.

In the main, two of the animal tumors employed in this investigation, i.e., mouse sarcoma No. 180 and rat carcinosarcoma No. 256, have not been very satisfactory for this purpose. This is due mainly to the fact that these tumors metastasize rarely, exitus in general being due to emaciation. The tumors are slowly growing so that experiments are time consuming, the growth rate rather erratic, and spontaneous remissions frequent. On the other hand, the Brown-Pearce rabbit epithelioma has offered an almost ideal tumor for study since its growth rate is uniformly rapid, the number of takes in the testis is high (98 per cent over a period of four years), it metastasizes from the testis with considerable uniformity in about ten days and exitus occurs on the average at approximately thirty-nine days. The number of spontaneous remissions is very small—less than 1 per cent. There is practically no seasonal variation, and it grows well in various strains of stock rabbits.

What may be considered the single massive lethal in vitro dosage for this tumor (with O. Sahler) lies in the range between 5,000 and 6,000 r, using 200 kv. These in vitro experiments indicate several interesting facts, the most important one being that if the tumor cells recover from smaller doses than this, so that the tumor transplant begins to grow, its growth rate is essentially that of untreated tumor cells, and the animal has the usual metastasis. The span of life from the time of the "appearance" of the irradiated (in vitro) tumor is not greatly increased over the control. One-third of the lethal amount is respon-

† This research has been aided by grants from the Rockefeller Foundation for Medical Research, and the International Cancer Research Foundation.

* From the Department of Medicine, Division of Radiology of the University of Rochester, School of Medicine and Dentistry and Strong Memorial Hospital, Rochester, N. Y.

sible for killing off about 20 per cent of the transplants. In general, the percentage of survivors of larger doses (that is, 3,000 to 4,000 r in vitro) is almost equally great. It is not until the sublethal amount of 5,000 r is reached that the number of surviving tumor transplants reaches a low level. Such an experiment as this irradiation in vitro emphasizes the tremendous amount of radiation necessary to cause direct and primary lethal damage to the tumor cells. This does not include of course the secondary deleterious effects upon the tumor cells which occur when the normal supporting stroma and other nearby body structures including blood vessels are damaged by irradiation in vivo. Perhaps if the skin of the rabbit were able to tolerate single massive doses of 2,000 to 5,000 r, it might be found that the tumor transplant could be killed by single massive doses of less than 5,000 r because of these secondary effects.

The next step is to investigate the in vitro effects of temperatures above normal body temperatures (with J. Jares). With mouse sarcoma No. 180, which was maintained in vitro at a constant temperature of 41.5° C., it was found that approximately fifteen hours were required for complete destruction of the viable tumor cells in all of the transplants while only eight hours were required at 42.0° C. With rat carcinosarcoma No. 256, thirteen hours were required at 41.5° C., and seven hours at 42.0° C. to prevent takes. With the Brown-Pearce rabbit epithelioma about thirty hours were required at 42.0° C., while at 43.0° C., in a single set of experiments, the time was reduced to approximately ten hours. The period required to kill all of this rabbit tumor in all the fragments at 41.5° C. in vitro was so long that the experimental data are unreliable. Part of the higher resistance of the rabbit tumor to these high temperatures may be explained by the higher normal body temperature of the rabbit whose rectal temperature fluctuates between 37.0 and 40.0° C.

The most difficult step is the application of these data in vivo. After a great many trials a method was developed (with J. Jares and O. Sahler) of raising the temperature locally in the testis tumor by means of a water bath for long periods of time without seriously inconveniencing the rabbit or disturbing the circulation of the tumor. It was found that it was impractical to establish an end point of time at a temperature of 42.0° C. in which all the tumor could be destroyed in all of the rabbits by the fever. There was, however, definite evidence that this temperature was effective in a great many cases in delaying the growth and spread of the tumor and in the longer experiments in developing a small percentage of cures. At 43.0° C., which is an impractical temperature for human cases, short treatments were destructive to this malignant tumor in vivo as well as in vitro.

The application of the combined radiations (roentgen and radiant energy) is fraught with great difficulties, chiefly because of the severe reactions which accompany large massive doses of roentgen radiation over the tumor-bearing site. Since the rabbit tumor grows best when transplanted in the testis, a region which is subject to considerable trauma from normal movements of the animal, any open lesions which develop are subject to soilage and secondary infection from urine and feces, and the cage bedding. Under normal conditions, skin in this part of the body can just tolerate 1,500 r in a single massive dose. Under good conditions, the epithelium will survive 2,000 r, so that with the massive dose we are limited to a level much below the in vitro lethal dose for these tumor cells. Under the very best conditions, the skin epithelium can survive eighteen hours at 42.5° C. plus between 1,500 and 1,700 r of roentgen radiation at 200 kv. This bath temperature produces a temperature of 42.0° C. in the center of the tumor. The roentgen radiation is calculated for the level of the middle of the tumor site so that some of the skin epithelium receives a little more and some a

little less, depending upon its position as determined by the various contours of the body. The probable variation is ± 1 per cent. The effectiveness of this combination is approximately twice as great in the number of cures of the local tumor as is obtained with either the same single massive dose of roentgen radiation alone or with the same amount of heat alone. Cure is determined by the local failure of the tumor to continue its growth, together with clinical disappearance of the tumor and failure to find evidence of viable-looking tumor cells upon histological examination. These experiments are greatly handicapped by the proclivity of the tumor to metastasize at a very early period—usually within a few days after it first becomes palpable, and a recognizable growing state determined. Since all of the treatment is restricted to the local site of transplantation (i.e., the testis), the longer observation is handicapped by the development of metastasis which we believe in many cases to have occurred before treatment was instituted.

It is obvious that even under the best of experimental conditions, the administration of massive doses of roentgen radiation and heat is not the solution of the problem since the percentage of cures is relatively low (40 per cent). Dividing up the exposure to radiant energy (to 42.5° C.) into multiple shorter local treatments with the massive dose of roentgen radiation seems to change the outcome very little.

The next step is to study the effect of simple fractional dosages of 200 kv. radiation. In brief, neglecting the units used, when the radiation was given daily, the simple fractional dosage technique gave slightly improved results over those previously used (45 per cent). This slight improvement may not be significant. A consideration of the different combinations of fractions of roentgen radiation and radiant energy dosage in both the simple and protracted forms is appalling because of the huge number of experiments necessary to establish a working basis. However, 76 experiments with a combination of simple fractional roentgen and radiant energy treatments given in immediate sequence daily show a very definite improvement in the destructive effects upon the tumors. Protracting the fractionated roentgen radiation in combination with the elevated temperature gives approximately the same effect. The percentage of clinical cures in both circumstances is elevated to between 80 and 90 per cent. The enhanced destructive effect is likewise evident with the combined use of protracted radium and fractional radiant energy treatments. Protraction of the roentgen (or radium) radiation seems to enhance the difference between the tolerance dose for skin, and that for tumor tissue in favor of the skin. The problem is too complicated to discuss at this point, especially since the definite relations of dosages—time and intensity and interval—are not well worked out.

While in general a tremendous amount of work has been done in this series of experiments, it must still be considered as a preliminary survey of the various dosage systems. Up to this point, it very definitely indicates a superiority of the fractional dose method of giving roentgen radiation over the single massive dose up to the tolerance of the normal tissues in each case. Likewise, there is the very definite indication that the combination of fractional roentgen radiation with repeated elevation of the tissue temperature is decidedly more effective in the destruction of the tumor within the tolerance of the normal tissues than either one of these radiations alone. These experiments illustrate that the summation of the radiation effects in the skin is far less than their summation in the tumor. However, the summation in the skin is important enough to warrant the warning that any adaptation of this principle to human cases must be accompanied by the precaution of staying well below the usual total dosage of roentgen radiation used in fractional therapy. The combination of an epithelitis and fever is apt to result in sloughing of the skin. A careful

study of this combination has been attempted in a few suitable cases with the full knowledge and consent of the patient. These preliminary studies seem to indicate that the skin will tolerate the combination of 300 r per day (up to 1,200 r per field) and two fever treatments, the first one of five hours at 41.5° C. rectal temperature given on the second day, the second one of one to five hours given on the fourth day, the radiation being given at the end of the fever while the patient's temperature is still 41.5° C. It should be pointed out that the radiation is given to the patient at the start of the cooling-off period so that the skin in the portal irradiated has been cooled down to a temperature well below 35.0° C. by the evaporation of the sweat on the surface, even though the rectal temperature and presumably the temperature of the tumor in the deeper structures beneath the skin has remained at somewhere between 41.0 and 41.5° C. during the irradiation. We have considerable evidence that would make us believe that during the treatment, while the rectal temperature is being maintained at 41.5° C., the tumor tissue, if it lies well beneath the skin, or in the deeper structures of the body has the same temperature (±0.1° C.) as the rectal temperature. From biopsy and autopsy material on 4 patients and clinical impressions from 2 others, there is definite evidence of a much greater destructive effect in the tumor which received both radiation and fever by this procedure than could be expected by either fever alone or roentgen radiation alone.

We cannot yet make a recommendation that such a dosage system should be tried out generally since disaster may result from the use of such a system in inexperienced hands. Nothing is known about the late changes which may occur in the skin and other parts of the body receiving radiation while the patient is in the febrile state. It is necessary to prospect the possibilities cautiously a step at a time and with the choice of suitable cases so that a comparison of the effects of the combined treatment alone may be made over a long period of observation, these results to be compared with the usual effect of roentgen radiation alone.

In conclusion, it is our definite impression from the animal experimental work and from the few patients that have cooperated with us in these studies that the effectiveness in destroying the tumor is greatly enhanced when fractional roentgen therapy is combined with fever therapy in the proper manner. We would like to make a plea for its use only after thorough consideration of the difficulty and risks involved.

ROSTER OF DR. GEORGE W. HOLMES' ASSOCIATES AND STUDENTS

THE following list contains the names of all the Assistant Roentgenologists, Residents, Graduate Assistants, and Graduate Students, who have served in an official capacity, on the Staff of the Department of Roentgenology of the Massachusetts General Hospital for six months or longer. This list does not include the numerous other Graduate Students who served for shorter periods without official appointments.

ASSISTANT ROENTGENOLOGISTS

Present Address	*Present Hospital and University Affiliations*
Adelbert S. Merrill, M.D. 814 Elm Street Manchester, New Hampshire	Roentgenologist, Elliot Hospital, Manchester, New Hampshire Private Practice, Manchester, New Hampshire
Resident: September, 1915 to September, 1916 Assistant Roentgenologist: September, 1916 to May, 1924	
James F. Boyd, M.D. 105 Waterman Street Providence, Rhode Island	Roentgenologist, Rhode Island Hospital Providence, Rhode Island
Graduate Assistant: August, 1917 to November, 1917 Acting Assistant Roentgenologist: November, 1917 to January, 1920	
John D. Camp, M.D. The Mayo Clinic Rochester, Minnesota	Associate Roentgenologist, Mayo Clinic Rochester, Minnesota Associate Professor of Radiology, Mayo Foundation, University of Minnesota
Graduate Assistant: July and August, 1918 and 1919 Assistant Roentgenologist: May, 1924 to September, 1927 Visiting Roentgenologist: September, 1927 to September, 1928	
Richard Dresser, M.D. Collis P. Huntington Memorial Hospital Boston, Massachusetts	Roentgenologist, Collis P. Huntington Memorial Hospital Consulting Roentgenologist, Palmer Hospital Roentgenologist, Pondville Hospital, (Mass. Dept. Public Health) Consulting Roentgenologist, Memorial Hospital, Worcester, Massachusetts Research Fellow in Roentgenology, Harvard Medical School
Graduate Assistant: February, 1923 to November, 1923 Assistant Roentgenologist: November, 1923 to September, 1929	
Aubrey O. Hampton, M.D. Massachusetts General Hospital Boston, Massachusetts	Assistant Roentgenologist, Massachusetts General Hospital Instructor in Roentgenology, Harvard Medical School
Resident: October, 1926 to October, 1927 Assistant Roentgenologist: October, 1927 to present	
Leslie K. Sycamore, M.D. Mary Hitchcock Hospital Hanover, New Hampshire	Roentgenologist, Mary Hitchcock Hospital, Hanover, New Hampshire Docent in Roentgenology, Dartmouth Medical School, Hanover, New Hampshire
Resident: September, 1928 to September, 1929 Assistant Roentgenologist: September, 1929 to September, 1930	
William Curry Martin, M.D. 902 Brown Building Louisville, Kentucky	Private Practice, Louisville, Kentucky
Graduate Assistant: March, 1928 to September, 1928 Assistant Roentgenologist: September, 1930 to September, 1935	
James R. Lingley, M.D. Massachusetts General Hospital Boston, Massachusetts	Assistant Roentgenologist, Massachusetts General Hospital Roentgenologist, McLean Hospital, Waverly, Massachusetts Roentgenologist, Harvard Department of Hygiene, Cambridge, Massachusetts Roentgenologist, Norfolk Prison Colony Hospital, Norfolk, Massachusetts
Resident: August, 1930 to August, 1931 Assistant Roentgenologist: June 1, 1931 to present	
Richard Schatzki, M.D. Massachusetts General Hospital Boston, Massachusetts	Assistant Roentgenologist, Massachusetts General Hospital, Boston, Massachusetts Instructor in Roentgenology, Harvard Medical School
Graduate Assistant: September, 1933 to September, 1935 Assistant Roentgenologist: September, 1935 to present	

RESIDENTS

Sherwood Moore, M.D.
510 South Kingshighway Blvd.
St. Louis, Missouri
Professor of Radiology, Medical School, Washington University
Director of Radiology, Edward Mallinckrodt Institute, St. Louis, Missouri
Resident: July, 1916 to February, 1917

Elba D. McCarty, M.D.
Hoquim General Hospital
Hoquim, Washington
Roentgenologist, Aberdeen General Hospital, Aberdeen, Washington
Hoquim General Hospital, Hoquim, Washington
Resident: April, 1917 to April, 1918

Herman A. Osgood, D.M.D., M.D.
144 Commonwealth Avenue
Boston, Massachusetts
Private Practice, Dental Radiology, Boston, Massachusetts
Resident: July, 1918 to July, 1919

Charles L. Martin, M.D.
Baylor Hospital
Dallas, Texas
Professor of Radiology, Baylor Medical School,
Director of Department of Radiology, Baylor Hospital, Dallas, Texas
Resident: July, 1919 to June, 1920

Ross Golden, M.D.
Presbyterian Hospital
New York City
Director, Department of Radiology, Presbyterian Hospital, New York City
Professor of Radiology, College of Physicians and Surgeons, Columbia University, New York City
Resident: May, 1920 to May, 1921

David S. Dann, M.D.
440 Argyle Building
Kansas City, Missouri
Private Practice of Radiology, Kansas City, Missouri
Chief Radiologist, Menorah Hospital, Kansas City Hospital (General), Alfred Benjamin Dispensary, Kansas City, Missouri
Acting Resident: May, 1921 to May, 1922

Max Ritvo, M.D.
485 Commonwealth Avenue
Boston, Massachusetts
Private Practice of Roentgenology, Boston, Massachusetts
Visiting Roentgenologist, Boston City Hospital
Visiting Roentgenologist, Beth Israel Hospital, Boston, Massachusetts
Instructor in Roentgenology, Harvard Medical School
Assistant Professor of Roentgenology, Tufts Medical School
Resident: May, 1922 to July, 1923

Robert G. Vance, M.D.
264 Beacon Street
Boston, Massachusetts
Private Practice of Roentgenology, Boston, Massachusetts
Roentgenologist, Newton Hospital, Chelsea Memorial Hospital, Winchester Hospital, Framingham Hospital
Assistant Visiting Roentgenologist, Massachusetts General Hospital
Resident: June, 1923 to June, 1924

David Steel, M.D.
St. John's Hospital
Cleveland, Ohio
Roentgenologist, St. John's Hospital, Cleveland, Ohio
Roentgenologist, Evangelical Deaconess Hospital, Cleveland, Ohio
Resident: June, 1924 to June, 1925

Robert J. Reeves, M.D.
Duke University
Durham, North Carolina
Roentgenologist, Duke University Hospital
Professor of Roentgenology, Duke University, Durham, North Carolina
Resident: June, 1925 to June, 1926

William A. Fuson, M.D.
905½ Main Street
Trenton, Missouri
Private Practice, Trenton, Missouri
Resident: June, 1926 to June, 1927

Langton T. Thaxter, M.D.
Maine General Hospital
Portland, Maine
Roentgenologist, Maine General Hospital, Portland, Maine
Resident: June, 1927 to June, 1928

John J. Winkler, M.D.
2930 Prospect Avenue
Cleveland, Ohio
Formerly associated with Doctors Hill and Thomas, Cleveland, Ohio. Not in Practice
Resident: September, 1927 to September, 1928

Clarence N. McPeak, M.D.
18 Hartwell Street
Fitchburg, Massachusetts
Private Practice of Radiology, Fitchburg, Massachusetts
Roentgenologist, Henry Heywood Memorial Hospital, Gardner, Massachusetts
Roentgenologist, Addison Gilbert Hospital, Gloucester, Massachusetts
Consultant Roentgenologist, Gardner State Hospital
Resident: June, 1928 to June, 1929

Marcy L. Sussman, M.D.
Mount Sinai Hospital
New York City
Associate Roentgenologist, Mount Sinai Hospital, New York City

Resident: June, 1929 to June, 1930

Cornelius V. Kilbane, M.D. — Formerly Roentgenologist, Doctor's Hospital, New York City. Died December, 1935

Resident: September, 1929 to September, 1930

Charles E. Dumas, M.D.
390 Main Street
Worcester, Massachusetts
— Private Practice of Radiology, Worcester, Massachusetts
Assistant Roentgenologist, Pondville Hosp., Norfolk, Massachusetts
Assistant Radiologist, Boston Dispensary and Tufts Medical School, Boston

Resident: June, 1930 to June, 1931

Edward L. Voke, M.D.
256 West Cedar Street
Akron, Ohio
— Roentgenologist, Peoples Hospital, Akron, Ohio
Citizens' Hospital, Barberton, Ohio

Resident: January, 1931 to January, 1932

Ralph B. Miller, M.D.
346 North Central Avenue
Glendale, California
— Private Practice of Radiology, Glendale, California

Resident: July, 1931 to July, 1932

Arthur B. Soule, M.D.
Mary Fletcher Hospital
Burlington, Vermont
— Roentgenologist, Mary Fletcher Hospital, Burlington, Vermont
Roentgenologist, St. Albans Hospital, St. Albans, Vermont
Assistant Professor of Pathology, University of Vermont College of Medicine

Resident: March, 1932 to July, 1932

Graduate Assistant: July, 1932 to September, 1932

Herbert A. Shaffer, M.D.
Beckley Hospital
Beckley, West Virginia
— Roentgenologist, Beckley Hospital, Beckley, West Virginia

Resident: July, 1932 to January, 1933

Stevens S. Sanderson, M.D.
868–868A Maccabees Building
Detroit, Michigan
— Private Practice of Radiology, Detroit, Michigan

Resident: July, 1933 to July, 1934

E. Gerard Smith, M.D.
St. John's Hospital
Cleveland, Ohio
— Assistant Roentgenologist, St. John's Hospital, Cleveland, Ohio

Resident: January, 1933 to January, 1935

Jack Spencer, M.D.
Collis P. Huntington Memorial Hospital
Boston, Massachusetts
— Assistant Roentgenologist, Collis P. Huntington Memorial Hospital
Assistant Roentgenologist, Palmer Memorial Hospital, Boston
Research Fellow in Medicine, 1935–1936, Harvard Medical School, Boston
Research Fellow in Roentgenology, 1936–1937, Harvard Medical School, Boston

Resident: July, 1933 to July, 1934

J. M. Robinson, M.D.
Massachusetts General Hospital
Boston, Massachusetts

Graduate Assistant, July, 1932 to August, 1933

Resident: July, 1934 to July, 1936

Harold O. Peterson, M.D.
University Hospital, University of Minnesota
Minneapolis, Minnesota
— Assistant Roentgenologist, University Hospital, University of Minnesota, Minneapolis, Minnesota

Resident: January, 1935 to January 1, 1937

GRADUATE ASSISTANTS

John Sproull, M.D.
50 Merrimack Street
Haverhill, Massachusetts
— Roentgenologist, Gale Hospital, Haverhill, Massachusetts

Graduate Assistant: 1918 to 1919

Alexander S. MacMillan, M.D.
483 Beacon Street
Boston, Massachusetts
— Private Practice of Roentgenology
Roentgenologist, Massachusetts Eye and Ear Infirmary
Assistant in Roentgenology, Harvard Medical School

Graduate Assistant: October, 1918 to October, 1919

Roy G. Giles, M.D.
Scott and White Clinic
Temple, Texas
— Roentgenologist, Scott and White Clinic, Temple, Texas

Graduate Assistant: November, 1920 to May, 1921

Karl F. Kesmodel, M.D.
701 Medical Arts Building
Birmingham, Alabama
Private Practice of Radiology, Birmingham, Alabama
Radiologist, St. Vincent Hospital, South Highlands Infirmary, Children's Hospital, Crippled Children's Clinic; Anti-Tuberculosis Clinic, Birmingham Baptist Hospital, Hillman Hospital, Birmingham, Alabama
Graduate Assistant: November, 1920 to May, 1921

Harry L. Farmer, M.D.
10515 Carnegie Avenue
Cleveland, Ohio
Private Practice of Roentgenology, with Drs. Hill, Thomas, Farmer and Sacket, Cleveland, Ohio
Visiting Roentgenologist, Cleveland City Hospital
Roentgenologist, Huron Road Hospital
Graduate Assistant: August, 1921 to August, 1922

Merrill C. Sosman, M.D.
Peter Bent Brigham Hospital
Boston, Massachusetts
Roentgenologist, Peter Bent Brigham Hospital, Boston
Consulting Roentgenologist to Collis P. Huntington Memorial Hospital, Children's Hospital, N. E. Peabody Home for Crippled Children and Boston Psychopathic Hospital
Assistant Professor of Roentgenology, Harvard Medical School
Graduate Assistant: September, 1921 to September, 1922

Carroll E. Cook, M.D.
30 North Michigan Avenue
Chicago, Illinois
Roentgenologist, 30 North Michigan Avenue, Chicago, Illinois
Roentgenologist, Chicago Municipal Tuberculosis Sanitarium
Graduate Assistant: July, 1922 to December, 1922

Dorrance Sheffield, M.D.
St. Johnsbury, Vermont
Private Practice, St. Johnsbury, Vermont
Graduate Assistant: July, 1923 to November, 1923

Kingsley Blake, M.D.
415 West 51st Street
New York City
Roentgenologist, American Hospital, Beirut, Syria
Assistant in Medicine, American College, Beirut, Syria
Graduate Assistant: December, 1923 to December, 1924

Cornelius O. Bailey, M.D.
727 West Seventh Street
Los Angeles, California
Instructor in Roentgenology (Radiotherapy), College of Medical Evangelists, Los Angeles, California
Graduate Assistant: May to September, 1924

David S. Beilin, M.D.
Augustana Hospital
Chicago, Illinois
Radiologist, Augustana Hospital, Chicago, Illinois
Graduate Assistant: September, 1924 to August, 1925

Philip D. Batchelder, M.D.
188 Waterman Street
Providence, Rhode Island
Private Practice, Providence, Rhode Island
Assistant Roentgenologist, Rhode Island Hospital, Providence, Rhode Island
Graduate Assistant: September, 1924 to August, 1925

John Russell Carty, M.D.
New York Hospital
525 East 68th Street
New York City
Radiologist to the New York Hospital
Associate Professor of Radiology, Cornell University Medical School, New York City
Graduate Assistant: April, 1925 to October, 1925

Stafford L. Warren, M.D.
Strong Memorial Hospital
Rochester, New York
Assistant Professor, The University of Rochester School of Medicine and Dentistry, 1925–1929; Associate Professor of Medicine in Charge Division of Radiology
Graduate Assistant: August, 1925 to August, 1926

Joseph H. Lucinian, M.D.
403–4 Huntington Building
Miami, Florida
Private Practice of Roentgenology, Miami, Florida
Chief Roentgenologist, Victoria Hospital; Visiting Roentgenologist, Jackson Memorial Hospital
Graduate Assistant: September, 1925 to March, 1926

Melson Barfield-Carter, M.D.
805 Woodward Building
Birmingham, Alabama
Private Practice of Roentgenology, Birmingham, Alabama
Roentgenologist part time, West End Hospital; Gorgas Hospital, Hillman Hospital, and Crippled Children's Hospital
Graduate Assistant: June, 1926 to June, 1927

Henry W. Grady, M.D.
Medical Corps, U. S. Army
Walter Reed General Hospital
Washington, D. C.
Roentgenologist, Walter Reed General Hospital, Washington, D.C.
Graduate Assistant: June, 1927 to December, 1927

Norman W. Loud, M.D.
New Britain General Hospital
New Britain, Connecticut
Roentgenologist and Laboratory Director, New Britain General Hospital, New Britain, Connecticut
Graduate Assistant: 9 months in 1928–1929 and 3 months in 1930

William H. VanWart, M.D. — Private Practice, Hartford, Connecticut
650 Main Street
Hartford, Connecticut
Graduate Assistant: 1929 to 1930

Hugo Roesler, M.D. — Cardiologist, Temple University Hospital; Associate Professor of Roentgenology, Temple University Medical School
Temple University Hospital
Philadelphia, Pennsylvania
Graduate Assistant: October, 1930 to April, 1931

Harold Thomas, M.D. — Chief, Hwa Mei Hospital, Ninopo Chekiang Province, China
368 Highland Avenue
Wollaston, Massachusetts
Graduate Assistant: April, 1931 to August, 1931

William J. Elliott, M.D. — Roentgenologist, Memorial Hospital, Worcester, Massachusetts
119 Belmont Street
Worcester, Mass.
Graduate Assistant: July, 1933 to July, 1935

Savvas E. Theodorides, M.D. — Private Practice, Boston, Massachusetts
315 Huntington Avenue
Boston, Massachusetts
Graduate Assistant: January, 1935 to January, 1936

Roland D. Clapp, M.D.
15 Monument Street
Medford, Massachusetts
Graduate Assistant: July, 1935

GRADUATE STUDENTS

John Meachem, M.D. — Roentgenologist, Cambridge Hospital, Massachusetts Women's Hospital, Free Hospital for Women and Parkway Hospital, Brookline, Leonard Morse Hospital, Natick, Weymouth Hospital, Weymouth and Emerson Hospital, Concord
475 Commonwealth Avenue
Boston, Massachusetts
Visiting Roentgenologist, Lawrence Memorial Hospital, Medford
Visiting Roentgenologist: January, 1926 to January, 1934

Herbert A. Judson, M.D. — Assistant Roentgenologist, Los Angeles County Hospital, Los Angeles, Roentgenologist, Ross-Loos Medical Group, Los Angeles
547 Burlingame Avenue
Brentwood Heights
Los Angeles, California — Instructor in Medicine (Radiology), University of Southern California School of Medicine
Graduate Student: September, 1930 to April, 1931

James R. Gemmill, M.D. — Private Practice, Monessen, Pennsylvania
130 Seventh Street
Monesson, Pennsylvania
Graduate Student: October, 1930 to April, 1931

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Publisher: CHARLES C THOMAS, 220 East Monroe St., Springfield, Illinois.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich. Office of publication 220 E. Monroe St., Springfield, Ill. Information of interest to all readers will be found on page iv.

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Representative on The American Board of Radiology: L. R. Sante, St. Louis, Mo., B. R. Kirklin, Rochester, Minn., W. F. Manges, Philadelphia, Pa.

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Member, National Research Council: Henry J. Walton, Baltimore, Md.

Editor: Lawrence Reynolds, 110 Professional Building, Detroit, Mich.

Assistant Editor: Ruth Bigelow, 110 Professional Building, Detroit, Mich.

Editorial Board: A. C. Christie, E. H. Skinner, Lauriston S. Taylor.

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Janeway Lecture Committee: Curtis F. Burnam, Chairman, Baltimore, Md.

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Representative on The American Board of Radiology: Rollin H. Stevens, Detroit, Mich.

Twenty-second Annual Meeting: Hotel Chelsea, Atlantic City, N. J., June 7–8, 1937.

EDITORIAL

THE INFLUENCE OF GEORGE W. HOLMES ON ROENTGENOLOGY

THERE is a happy custom, unfortunately one more honored in the breach than in the observance, of appreciative students from time to time issuing what the Germans call a *Festschrift* commemorating some anniversary in the life of a beloved teacher. The former and present pupils of George W. Holmes have seized upon a combination of events, namely, his sixtieth birthday and the twenty-fifth anniversary of his directorship of the Department of Roentgenology of the Massachusetts General Hospital, to do honor to one who so justly deserves it. During these twenty-five years Holmes has stood at the forefront of his profession, making untold contributions to the advancement of roentgenology. These contributions have taken two forms: first, that dealing with the scientific aspect of his profession as expressed in his various writings on the subject. This form can be measured to a more or less accurate degree; the other is an intangible something which he has imparted to the students who have year in and year out passed through his department and have gone out imbued with the spirit and character of the teaching which George Holmes has given them. They have scattered to the four corners of the world and wherever they are have carried on with the same high degree of scientific endeavor which they so admirably learned under his tutelage. This intangible quality of medical teaching does not lend itself to measurement but represents in its essence teaching of the highest order.

What is it that enables one man to be of such a force in the furtherance of a high calling such as teaching? What are the prerequisites of a great teacher? It is not alone his accumulated knowledge that he is able to express in well chosen words; it is not alone his example in his contacts in the daily professional life; it is over and above all that inexplicable something called inspiration. This enables a teacher to so mold the lives and characters of a group of pupils as to influence them toward the better and finer things in the profession. Such a teacher is George Holmes. He has not only the ability to think, to write and to work, but he has a fourth quality to add to his many facetted character, that of an inseminator of minds. It is not necessary in this editorial to call attention to his methods of instruction. While all men who teach follow a similar plan of assembling a subject under the various divisions, subdivisions, class room talks and conferences, the teaching of George Holmes transcends this routine. After all it is the harvest that is the sure test of what the sowing and tending of the crop has been, and measured by this standard George Holmes ranks among the highest in his chosen profession.

Emerson once said: "For a time, our teachers serve us personally, as metres or milestones of progress. Once they were angels of knowledge, and their figures touched the sky. Then we drew near, saw their means, culture, and limits; and they yielded their place to other geniuses. Happy, if a few names remain so high that we have not been able to read them nearer, and age and comparison have not robbed them of a ray." Truly, George Holmes is of this class. The closer contacts, the more frequent meetings with him, not only do not dim the ray of his mind nor blur the outline of his personality but only serve to enhance it, and he represents, as has been said of other great men, the "moral radium" of the medical world. The AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY is indeed honored in being the medium through which the students of George Holmes have elected to pay him homage.

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VOLUME 36 DECEMBER, 1936 NUMBER 6

JAN 4 1937

[FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY]

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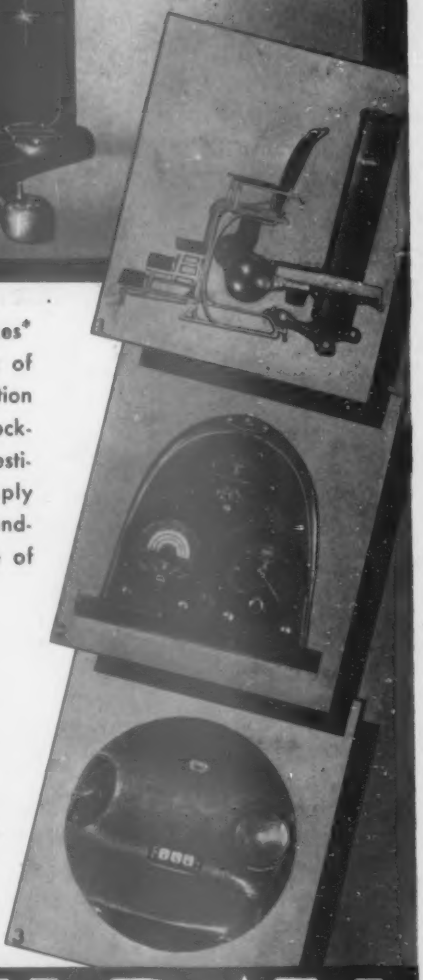


THE WAITE SHOCKPROOF THERAPY UNIT

is installed in such institutions as

MAYO CLINIC†
Rochester, Minnesota

PRESBYTERIAN MEDICAL CENTER†
New York City

MASS. GENERAL HOSPITAL
Boston, Mass.

UNIVERSITY OF IOWA
Iowa City, Iowa

UNIVERSITY OF CHICAGO
Chicago, Illinois

MT. SINAI HOSPITAL
New York City

UNIVERSITY HOSPITAL
Baltimore, Maryland

UNIVERSITY OF VIRGINIA
Charlottesville, Va.

JOHNS HOPKINS HOSPITAL
Baltimore, Maryland

DUKE UNIVERSITY HOSPITAL
Durham, North Carolina

CLEVELAND CITY HOSPITAL†
Cleveland, Ohio

BELLEVUE HOSPITAL†
New York City

WALTER REED HOSPITAL
Washington, D. C.

VETERANS ADMINISTRATION FACILITY†
Hines, Illinois

UNIVERSITY OF ROCHESTER
Rochester, N. Y.

**The names of approximately 100 prominent users of Waite Shockproof Therapy equipment will be sent to you upon request.*

††Two or more complete installations.

Set forth on this page are names* comprising a veritable Blue Book of American Roentgenology. Their selection and installation of the new Waite Shockproof Therapy Unit, after careful investigation of all available makes, amply attest to its superior construction, dependability, flexibility, safety and ease of operation.

A few outstanding features of the Waite Therapy Unit

Flexibility permitting every conceivable angle for treatment from above or below the patient.

A set of variable filters permanently installed in the shockproof head, (fig. 3) with automatic registration (fig. 2) at the control stand to give an absolute check at all times as to what filters are being used.

All high tension parts, including x-ray tubes, valve tubes, hermetically sealed in oil, assuring constant efficient operation, regardless of climatic conditions.

PICKER X-RAY

WAITE EQUIPMENT PICKER ACCESSORIES

300 FOURTH AVENUE, NEW YORK
540 N. Michigan Ave., Chicago 10515 Carnegie Ave., Cleveland Representatives Everywhere

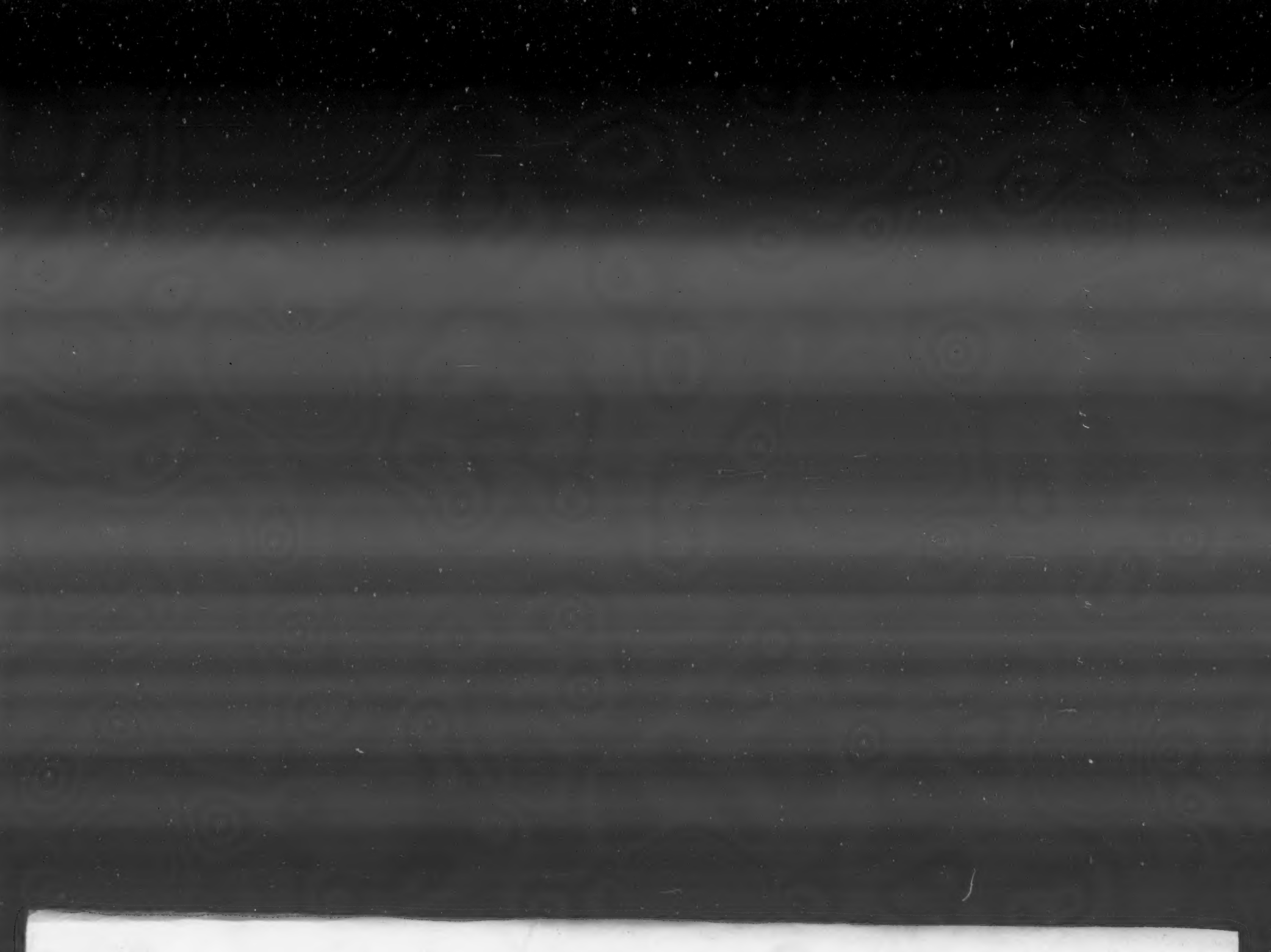
1917...The Potter-Bucky Diaphragm

Radiograph of sacral spine made without the Potter-Bucky diaphragm.

Radiograph of the same patient made with the Potter-Bucky diaphragm.

The prevention of scattered radiation from reaching the recording medium during exposure became possible with the development of the Potter-Bucky diaphragm. Thus, for the first time, secondary radiation generated by the thicker body parts could be effectively controlled. The result was radiographic images of greater contrast and diagnostic detail.

THE Potter-Bucky diaphragm was an outstanding mechanical achievement in the progress of radiography. But its extensive use did not become practical until the introduction of Dupli-Tized film and the double screen technic. This double-coated film was one of the important contributions of Eastman research on radiographic recording media, which commenced with the discovery of the x-rays.

Today there is Eastman *Ultra-Speed* Safety X-ray Film with every characteristic demanded by modern technic. Sensitivity is adequate for split-second exposures, yet there is latitude to compensate slight errors in judging the patient. Brilliant contrast or maximum detail with moderate contrast, as required, can be recorded. Each film is exactly like the last, exactly like the next. With Eastman *Ultra-Speed* Film the economy and efficiency of standardized technic are easily achieved. Eastman Kodak Co., *Medical Division*, Rochester, N. Y.

EASTMAN ULTRA-SPEED SAFETY X-RAY FILM